SYNOPSIS OF
TROPICAL MEDICINE

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PREFACE TO THE THIRD EDITION

Four years have elapsed since the publication of the second edition of this Synopsis During this time there have been many advances to record in the field of treatment as well as of prophylaxis of the diseases of the tropics

Tropical Medicine has now become a very large subject and therefore more difficult to keep track of in all its branches and although there have been no sensational developments to record on this occasion comparable to those enunciated in the last edition advances have been numerous

The number of drugs and antibiotics in the Tropical Pharmacopoeia has greatly increased so much so that it has become necessary to create a special section for their tabulation It takes the place formerly held by a synoptic description of special laboratory methods which have now been outmoded This drug table has been arranged in alphabetical order with indications and dosages thus forming an ever ready and handy reference for treatment It is hoped that this useful feature may prove of advantage to those who have neither the time nor the opportunity of consulting the larger works on Tropical Medicine

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PREFACE TO THE FIRST EDITION

This synopsis has been undertaken in response to numerous requests to provide a guide to tropical medicine in a condensed form suitable for medical officers in the Armed Forces and others whom the exigencies of the moment call to the tropics

Though not designed in any way to encroach upon standard textbooks on tropical medicine this work will it is hoped provide adequate information in convenient compass The material has as far as possible been brought up to date and the revision has been undertaken as a small contribution to the war effort

This task would have been impossible without the aid of those invaluable publications the *Tropical Diseases Bulletin Bulletin of Hygiene* and *Bulletin of War Medicine*

My thanks are due to my colleague Lt Col F Murgatroyd R A M C for undertaking the task of proof correction

Philip Manson Bahr

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CHAPTER I

PROTOZOAL DISEASES

MALARIA

Note —B T = Benign tertian O T = Oval tertian Q = Quartan
S T or M T = Subtertian E E = Exo-erythrocytic cycle

This is the most important tropical fever and is due to four distinct parasites benign tertian ovale tertian quartan and subtertian.

GEOGRAPHICAL DISTRIBUTION

Benign Tertian is widespread in Europe as far as 60 N and occurred in England until comparatively recently but is still found in Holland and N Germany in N America in the valley of Sacramento at 40° N Its southern range is less extensive to Natal Brazil 30 S and to S limits of Argentine at 40 S It is found rarely (in Himalayas) above 6 000 ft

Ovale Tertian closely allied to above is common in West and Central Africa isolated cases reported from E Russia Egypt Palestine Mauritius Philippines Venezuela India and New Guinea

Quartan is restricted and local occasionally found in temperate climates in N Europe in Mediterranean S Italy Greece Macedonia Palestine Iraq S India Maldive Islands Andaman Islands Ceylon Malaya sparsely in tropical and subtropical Africa West Indies (Antigua) Brazil Panama In endemic areas it is found especially in children

Subtertian (or Malignant) has a tropical and subtropical distribution corresponding to the summer isotherm of 70 F (21 C) and winter isotherm of 48° F (9 C) in Europe S Italy Macedonia N Africa Jordan Valley Palestine It is dominant throughout tropical W and Central Africa and has a restricted distribution in the plains of Central and S India the Duars and Himalayan foothills S Malaya Dutch E Indies New Guinea N Australia Queensland New Hebrides and Solomon Islands in the New World in the West Indies Panama Brazil In Kenya in Londiani

PLATE I

MALARIA PARASITES (Leishman stained)

Benign Tertian (*Plasmodium vivax*)

1 —Ring form
2 —Quarter grown form
3 —Half grown form
4 —Gametocyte
5 —Sporulating body

artan (*P malariæ*)

—Ring form
—Quarter grown form
3 —Half grown form
4 —Gametocyte
5 —Sporulating body

Ovale Tertian (*P ovale*)

1 —Ring form
2 —Half grown form
3 —Young gametocyte
4 —Gametocycte
5 —Sporulating body

Subtertian (*P falciparum*)

1 —Young ring and accolé forms
2 —Ring form and Maurer s clefts or spots
3 —Half grown form and Maurer s clefts
4 —Gametocyte (crescent)
5 —Sporulating body






Ben gn Te t an (B T) (P asmod um e)






Qua t an (Q) (P m ar ae)






O a e Te t an (O T) (P ovae)






Sub rtian (S T) (P falc pa um)

Plate I. Malaria Parasites

capillaries the parasites in spleen liver and bone-marrow are small solid stain deeply and show no vacuoles Sporulating forms (0·75–0·8 μ) are rarely seen in blood mostly in the internal organs especially in brain capillaries Merozoites are small (0·75–0·8 μ) about 32 in number Sporulation (schizogony) does not proceed at the uniform rate of other types After 48 hours gametocytes (crescents) are produced in cells in the internal organs At first solid and round without vacuoles they become crescent shaped (more like sausages with rounded ends) 9–14 μ by 2–3 μ across (at this stage Garnham's rod —inclusion body—dark red straight or twisted into loop or coil may be seen—like Cabot's ring) Crescents appear after an infection has lasted 2–3 weeks and may persist for six weeks after subsidence of fever The life span of the crescent is 2–3 weeks *Male* crescent (gametocyte) is broader and stumpier with diffuse nucleus and scattered pigment *Female* stains more deeply is more slender and has chromatin and pigment concentrated Young sexual cells can be distinguished from schizonts of same age by their elongated shape and diffuse pigment the nucleus (chromatin) is small and placed towards one end There are varieties of *P falciparum* some more virulent than others The large ring form is said to predispose to blackwater fever *P tenue* with more active amoeboid movement may be a sub species The subtertian has a much shorter life span in human blood than other species A single infection persists for one month to one year

Strains of *P falciparum* have been separated from W Africa Belgian Congo Italy and Roumania They vary in virulence in susceptibility to quinine and ability to develop anopheles mosquitoes—*A maculipennis atroparvus*

Exogenous cycle in Mosquito (Anopheles)—In blood outside body or in stomach of mosquito the male sexual cells (*microgametocytes*) exflagellate with six flagella (*microgametes*) The subtertian crescent first becomes round the pigment undergoing agitation The female (*macrogametocyte*) also becomes rounded and quiescent The *microgametes* break away and fertilize the female macrogametocyte which then becomes a *zygote* After impregnation the cell becomes oval elongated and capable of independent movement (travelling vermicule or *oökinete*) bores its way into the lining epithelium of the mosquito's stomach and becomes an *oöcyst* The original nucleus develops rapidly and the protoplasm also segments forming a spongioplasm from which *sporozoites* are formed The cyst bursts and liberates sporozoites which enter the salivary glands and are injected by mosquito into blood of man with salivary secretion The sporozoites then enter the liver cells where they undergo a tissue stage or E E cycle

Under optimum conditions the exogenous cycle in the mosquito takes 8–10 days but is subject to great variation and is dependent upon temperature and moisture The optimum conditions are a constant temperature of 68–80 F (20 C–27 C) in association

with mean relative humidity of 60 per cent. or more Higher peratures are usually necessary for *P falciparum* As a it takes 10 days for anopheles to become infective with *P* 15 days with *P ovale* Development ceases at a con tant perature of 60° F (16 C) At 68° F (20° C) the cycle occ 16 days for *P vivax* 22 for *P falciparum* 32 for *P malariæ*

There are minor differences in the oöcysts in different species the case of *P ovale* the arrangement of the pigment in the o is distinctive and the sporozoites are more slender and small

Exo erythrocytic (E E) Cycle—The sporozoites injected into ma the mosquito bite do not as postulated originally by Schau enter the red blood corpuscles and thus initiate the erythro (or blood) cycle of the parasite but as has been shown so effect by Shortt Garnham and others enter the liver cells where in course of 7–9 days (representing the incubation period of ma in man) they develop into a cyst containing large numbe merozoites (*cryptomerozoites*) which escape into the bloodstrea enter red blood corpuscles and thus to initiate the erythro cycle The forms within the liver are known as *cryptoschi* and this cycle is more properly designated the *pre erythro cycle* The mechanism of the malaria relapse is now expla by the entry of some cryptomerozoites into other liver cells w they multiply to form a reservoir so as to produce a relaps some future occasion This is properly known as the *erythrocytic* cycle These stages in the liver are pigmentless *P vivax* infections the fully developed cryptoschizont is 42 length and contains some 800 chromatin masses that of *falciparum* is even larger and contains more numerous *cry merozoites* As far as is at present understood in *P falcipa* the pre-erythrocytic development lasts about 7 days and *P vivax* 9 days whereas in the former development does proceed further than the pre-erythrocytic phase in *P viva* passes into the secondary phase and persists in the liver after parasites have gained access to the bloodstream

The characters of the tissue phase of *P ovale* differ from thos *P vivax* and *P* *inui* but more resemble that of *P falcipa* in size and form but whereas the *cryptoschi onts* of the s dimensions in *P falciparum* produce 40 000 small merozo *P ovale* produces a third of that number and of a larger s There is evidence of persistence of exo-erythrocytic schizog in this species as in *P vivax*

Congenital Malaria—benign quartan subtertian and ovale—h been recorded Exact manner in which the parasites enter placenta is not clear Unless due precautions are observed th is considerable risk in transmitting malaria by *blood transfusion*

PATHOLOGY

Accounts of pathology and morbid anatomy are based upon s tertian which is the most virulent and fatal Pathology of blackwa

fever is mainly exaggeration of same process *Pathology correlated to the I E cycle of the parasite*

Spleen birthplace and grave of malaria parasite is invariably enlarged (ague cake) and highly pigmented with hæmozoin (malaria pigment—hæmatin—formerly melanin) It shows destruction of effete red blood corpuscles by phagocytosis (macrophages—histiocytes) and storage of iron On section it is purple or chocolate colour with stretched capsule diffluent pulp pale grey Malpighian bodies immature parasites and pigmented monocytes in branches of splenic artery small infarctions and necroses

Liver is congested enlarged dark brown parenchyma cells contain no hæmozoin but hæmosiderin and bilirubin hæmozoin is deposited in Kupffer cells and parasites in congested sinusoids Changes are most marked in periphery of lobule Pigment persists in liver 3–4 months after disappearance of parasites

Kidneys are congested with grey dots and lines in pyramids due to parasites in Bowman s capsules convoluted tubules are affected and there are granular casts

Placental maternal sinuses are blocked with parasites

Brain and C N S—*Cerebral cases* Brain is lead-coloured with subcortical punctiform hæmorrhages Capillaries especially those of corpus striatum and callosum contain parasites *Areas of degeneration*—malarial granulomata—focal degeneration hæmorrhages and glial proliferation—are seen

CLINICAL PATHOLOGY

Blood shows rapid destruction of red blood corpuscles (count may fall below one million) poikilocytosis anisocytosis polychromasia basophilic stippling reticulocytosis monoblasts Cabot s rings and other signs of degeneration megalocytes occasional normoblasts clumping of red cells and increased sedimentation rate One parasite to 100 000 r b c necessary to produce symptoms There is hæmolysis of parasitized and also unparasitized cells Hæmozoin may act as hæmolysin Damage to reticulo-endothelium is important *Leucocytes* are increased in paroxysm subsequent leucopenia Relative increase of large mononuclears even after quinine treatment (15 per cent is diagnostic) may be pigmented diminution of blood platelets *Fluid elements* decrease in total protein *decrease in albumin increase of euglobulin and serum* bilirubin Indirect Van den Bergh reaction

Malaria pigment hæmozoin (hæmatin) is insoluble even in strong acids formed within parasites and contains firmly combined iron Hæmosiderin (derived from hæmoglobin destruction in parenchyma cells of liver spleen pancreas bone marrow connective tissue cells) contains free iron and gives Prussian blue reaction

Hæmofuscin iron free yellow is present in organs in chronic malaria Polycholia results from excessive blood destruction

Urine —Increased in amount chlorides and urea increased in ague phosphates decreased in rigor increased in sweating stage Transient albuminuria and glycosuria common Urobilinogen and urobilin increased as result of hæmolysis

General Statement —The number of parasites necessary to produce fever depends not so much on their prevalence as on the degree of tolerance of the host They differ in the first second and third relapses and so on Thus in the primary attack prolonged search may reveal no parasites on the first day and as long as the third On the other hand in relapse 3 000 or more may be found of which a considerable proportion may be gametocytes

CLINICAL FEATURES

Incubation period 10 days laboratory infection 14 days may lie latent for six months especially benign tertian more rarely subtertian Clinical appearances are greatly modified by the degree of immunity In hyperendemic areas it may produce no symptoms especially in *P falciparum* infections when parasites are present in numbers in the peripheral blood without fever

Premonitory Lassitude headache bone pains

Ague fit Rigor—cold stage 1–2 hours vomiting skin cold and blue temperature rises convulsions in children

Hot stage 3–4 hours feeling of warmth headache intense pulse full and bounding rapid respiration T 104–106 F

Sweating stage 2–4 hours sweating ++ feeling of relief T subnormal Herpes of lips and nose common

Spleen enlarges during rigor and is usually but not necessarily palpable especially in subtertian Liver enlarged and painful Typical ague in benign tertian quartan and ovale tertian seldom in subtertian

B T characterized by tendency to relapse after long quiescent intervals six months to one year Tertian periodicity with fever every 48 hours Initial fever may be irregular and uncharacteristic *O T* practically symptomless but may simulate subacute appendicitis or rheumatism In self induced *ovale* infections Garnham noticed severe attacks with irregular fever of rough tertian periodicity and persisting 3 weeks Persistent headache was a feature of short term relapses *Q* particularly persistent and symptomless with liability to *nephrosis*

S T great variations *e g* may be afebrile and symptomless or parasite may be latent for months Liability to explosions Rigor stage relatively less marked produces severe anæmia. Involvement of internal organs may simulate many other diseases

Forms of S T —*Bilious remittent* Severe fever bilious vomiting enlarged painful spleen and liver may resemble yellow fever or simulate typhoid (typhoid remittent)

Pernicious attacks hyperpyrexia delirium + coma mania epileptiform convulsions cerebral paralysis may resemble uræmic or

diabetic coma pontine hæmorrhage or cerebrospinal meningitis I sych al di turbances and loss of memory may ensue Many phenomena are physiological and due to anoxia

Algid forms Castric with vomiting epigastric pain sometimes hæmatemesis resembling gastric disease

Choleraic Profuse diarrhœa with collapse (peripheral vascular failure) simulating cholera

Dysenteric Blood and mucus in stools resembling bacillary dysentery

Purpuric Intradermal hæmorrhages

Oedematous General anarsarca resembling card ac beriberi

Syncopal Acute heart failure resembling card ac d ease

Acute anæmic Hæmolytic anæmia resembling pernicious anæmia

Nephritic Blood and casts in urine resembling acute nephritis

Gangrenous Gangrene of extremities may occur

Appendicular Pain in right il ac fossa resembling appendicitis

Cholecystitic Pain over gall bladder resembling acute cholecystitis

Icteric Deep jaundice resembling yellow fever Weil s disease or infective jaundice

S T malaria is particularly severe in children

SEQUELÆ

The main sequel is *Blackwater Fever* acute hæmolysis of red blood corpuscles liberating hæmoglobin which produces hæmoglobinuria pigment in urinary tubules and anuria Has same geographical distribution as subtertian malaria and occurs mostly in sensitized individuals *i e* those long resident in endemic zone and subjected to frequent infections with S T parasite Rare if ever after primary attack rate in natives of endemic zone unless protected from malarial infection in infancy as now in W Africa Cold exertion alcohol and excessive quinine predispose to attack It is now generally acknowledged that quinine is the chief excitant in the production of *hæmolysis* This is shown by the practical disappearance of blackwater since the introduction of modern antimalarials Malaria parasites are usually destroyed by hæmolysis but may persist malaria infection can be transmitted to non immune by blackwater blood Mechanism of hæmolysis not known possibly allergic

Hæmatin set free combines with serum albumin to form methæmalbumin stored in liver not excreted in urine Oxyhæmoglobin is converted into methæmoglobin which is excreted Mechanism of anuria is not due to blockage of urinary tubules as formerly supposed but to renal anoxia (Maegraith and Havard) on analogy with surgical shock cholera and renal failure In oliguria and anuria (tubulo vascular syndrome) kidney changes are produced by lack of oxygen resulting from alterations in the renal blood flow Great anæmia half r b c s destroyed Death from anoxæmia cardiac failure pernicious vomiting anuria Pathology resembles exaggerated sub tertian malaria with maximum onus on kidneys Histological changes resemble those of incompatible blood transfusion

CLINICAL —Enlarged painful spleen sudden onset rigor polyuria black (porter coloured) urine—methæmoglobinuria Bilious vomiting + hæmolytic icterus on 3rd day after which urine clears and contains bilirubin urobilin + and casts Suppression of urine on 8th day or later Death may occur later from convulsions coma or complications pneumonia streptococcal septicæmia etc Pigmented gallstones may be a sequel Relapses may occur one attack predisposes to second or third (usually fatal) but individuals may survive many attacks Retinal hæmorrhages may occur Death rate in Africa may be 50 per cent usually 25 per cent Blackwater fever not infrequent in temperate climates in malaria infected patients from tropics Has been seen in children is especially dangerous in pregnant women Those with predisposition to blackwater should not return to the tropics

Other sequelæ of malaria —Malarial cachexia splenomegaly (ague cake) retarded development in children Abortion in pregnant women Rupture of spleen *Splenic index* is guide to endemicity of malaria in district (50 per cent hyperendemic 25 per cent highly endemic 10 per cent moderately endemic) Spleen rate specially valuable in children *Parasite index* reliable up to five years of age less reliable afterwards

Immunity to malaria gradually acquired in childhood most adult natives relatively immune White man big fever black man little fever Balance between resistance to organisms and tendency of parasites to multiply = premunition Parasites frequently found in Africans otherwise in good health

DIAGNOSIS

Blood examination by thin and thick film methods latter is more reliable in mass surveys In quiescent period diagnosis by increase of mononuclears and pigmented leucocytes Diagnosis by therapeutic action of quinine or atebrin (mepacrine hydrochloride) or other antimalarials not recommended and only permissible when microscopic diagnosis is unobtainable

DIAGNOSIS BY CLINICAL SIGNS —Character of fever periodicity splenomegaly persisting urobilinuria patient s history (often unreliable) malaria rigors are simulated by genito-urinary and other infections Splenic and sternal puncture have been employed intravenous adrenaline may provoke attack. Blackwater to be distinguished from paroxysmal hæmoglobinuria Weil s disease (leptospirosis) favism and acute quinine poisoning

TREATMENT

The state of immunity naturally affects the use of antimalarial drugs and in these cases the dosages given below may require modification

Quinine efficacious in B T and in S T but may precipitate blackwater fever in latter Less effective in Q Quinine is to some extent superseded by introduction of synthetic drugs

Quinine sulphate is insoluble and acid sulph dil must be added to it hydrochloride fairly soluble dihydrochloride easily soluble and suitable for parenteral injection Lacquin (milk) preparation contains quinine ethyl carbonate with disguised taste is suitable for children

Dosage—Heroic doses inefficacious dangerous and do not extirpate infection Maximum dosage 30 gr (1·94 gm) Most infections react to 20 gr (1 29 gm) Children have 1/20th adult dose Rational dosage gr 30 for 3 days gr 20 for 7 days Anti relapse treatment gr 10 (0 64 gm) for 4 weeks

Toxic effects—*Quinine idiosyncrasy* dyspepsia urticaria skin sensitivity to scratch test *Quinine amblyopia* spasm of retinal artery blindness in overdosage In pregnancy very rarely may produce *miscarriage* In excessive doses quinine *hæmoglobinuria* resembling blackwater

Excretion of quinine in urine is controlled by Mayer Tanret reaction (mercuric chloride 27 gm in 1500 c c water pot iod 100 gm in 500 water mixed add 25 c c glacial acetic acid—turbidity produced) and by coating quinine tablets with methylene blue so that it is readily recognizable in urine of large groups

Injection of quinine Intramuscular into buttocks above gluteal fold gr to (1 64 gm) maximum Dissolve in 5 c c water inject slowly massage part Not more than three injections on successive days Dangers abscess septicæmia tetanus painful fibrotic nodules and when into sciatic nerve paralysis of leg

Intravenous quinine dihydrochloride for cerebral and algid forms of subtertian malaria Not more than 10 gr (0 64 gm) in 10 c c water (or 5 per cent glucose) combined with 10 min (0 6 c c) of 1 1000 adrenaline Inject *slowly*

Synthetic antimalarial drugs—*Atebrin* (mepacrine hydrochloride quinacrine)—yellow dye—specially indicated for S T gives effect comparable to quinine on rings (trophozoites) but not on gametocytes (crescents) effect on fever not so rapid as quinine Dose 1½ gr (0 1 gm) t d s for 7 days on full stomach For full cure repeat course after interval of 5 days In virulent S T cases combine with quinine atebrin 4½ gr (0 3 gm) quinine 10 gr (0 64 gm) daily In acute attack larger doses now advocated up to 0 9 gm for 2–3 days—not longer Atebrin staining of skin is necessary to obtain full effects

Atebrin by injection (atebrin musonate) intramuscularly or intravenously should be reserved for pernicious attacks of S T *Toxic effects* epigastric pain vomiting and yellow pigmentation of skin especially face and in susceptible individuals (Malays) cerebral excitement Skin eruptions and lichen planus of legs may ensue after prolonged atebrin therapy Maroon-coloured discolouration of base of nails is also a sign of chronic atebrin poisoning

Paludrine (*Proguanil* M 4888) is N p chlorophenyl N5 isopropylbiguanide acetate Acts on the E E forms This renders it an

PLATE III

LEISHMAN DONOVAN BODIES IN KALA AZAR AND RELATED FORMS

1 —Leishman Donovan bodies in endothelial cells in film from spleen puncture
2 —Free forms of Leishman Donovan bodies from spleen
3 —Developmental forms of *Leishmania donovani* from the leishman body to the crithidial stage and clumping of the flagellated organisms
4 —Parasites enclosed within splenic pulp cells as seen in section stained with hæmatoxylin
5 —Diagram of Leishman Donovan body greatly enlarged highly magnified

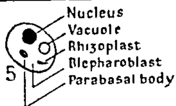
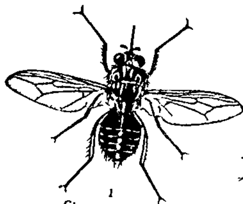


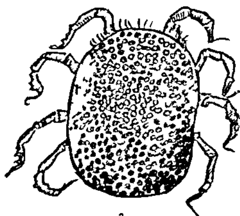
Plate III Leishman Donovan bodies in Kala azar and related forms



1
Glossina palpal s



2
Phlebotomus papatasii



3
Ornitl odor s moubata



4
Bull u contortus



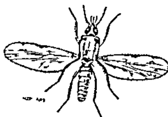
5
Planorbis bo ss j



6
Oncomelania nosopl ora



7
Simul urn damnosum



8
Culicoida austeni

Plate V Intermediary Hosts

Mediterranean—*L infantum* Associated with similar disease in dogs —*L caninum* Parasites of the reticulo-endothelium

Geographical distribution—India E Coast (epidemic and severe) Assam China N of Yangtse and in S China (Canton) Transcaspia Transcaucasia Turkestan S Manchuria S Sudan Italian Somaliland W Abyssinia N Kenya Darfur Chad Territory French Guinea and Congo Gambia Nigeria (rare) Morocco Tunis Algeria Persia Saudi Arabia Iraq and Egypt (rare) Brazil and Argentine Infantile form Mediterranean area Italy Sicily Greece Corsica Malta Aegean Islands Portugal S Spain Turkey Yugoslavia Palestine Transjordania Kala azar reported from France (Cherbourg Marseilles) and Hungary In S America widespread at first supposed to be new parasite—*L chagasi* (not accepted) Mexico Venezuela Colombia N Brazil Bolivia Paraguay

Association with dogs and other animals—Not invariable usually *in Mediterranean especially in Sicily Portugal and Turkestan* but canine leishmaniasis occurs in many areas notably Iraq where human disease is very rare Also canine disease is not *common in India and China where dogs are not notably affected* by it Jackals suspected in subtropical regions of Far Eastern Soviet Russia during reclamation of Vakhsh Valley in Tadjikistan where K A is a typical zoönosis In populated towns the disease has long been adapted to man whilst retaining its infectivity to dogs and is of the Mediterranean type with highest incidence among children In rural districts it is highest among adults

Transmission—Through sandfly in India *Phlebotomus argentipes* Final proof of transmission to man obtained by Christophers Shortt and others Transmission to hamsters (*Cricetus* and *Cricetulus*) also successful Possibly direct transmission by personal contact *via* nasal secretion L D bodies are found in nasal mucus also in urine (occasionally) and in fæces

SANDFLY TRANSMISSION

1 L D bodies undergo specific development in *Phlebotomus*

2 When fly is infective cannot take blood meal without inoculating leptomonad forms Infected sandflies bite voraciously in *P argentipes* the blockage of the œsophagus with developmental forms resembles fleas infected with *P pestis* (*q v*) (see p 86)

3 In *Phlebotomus* caught in K A houses leptomonads are found apparently derived from L D bodies

4 These forms are infective to hamsters (*Cricetulus*) by inoculation or by ingestion of flies

5 Actual transmission has been proved by bite of infected sandflies to hamsters and also to man

CONGENITAL TRANSMISSION of K A from mother to child recorded

K A attacks both sexes all ages recently arrived immigrants most readily In Mediterranean mostly attacks children aged 5 months to 10 years but adults also in India it affects all ages

PATHOLOGY

Body emaciated abdomen swollen Spleen grossly enlarged capsule thickened nodular Cartilaginous in chronic stages numerous infarctions *Congestion of spleen pulp one fifth composed of parasites* Liver enlarged brown mottled Pressure atrophy of parenchyma and eventually fine intralobular cirrhosis Parasites in Kupffer cells filled with parasites Gastro intestinal tract proliferation of reticulo-endothelial cells especially in duodenum and jejunum Villi hypertrophied and swollen packed with parasitized cells Lymphatic glands enlarged and congested L D bodies + Underlying essential pathology is blockage of reticulo endothelium Parasites engulfed by endothelial cells multiply until cell ruptures and organisms escape into blood stream and are carried to other organs

CLINICAL PATHOLOGY

Progressive anæmia of secondary type but when marrow is destroyed anæmia becomes of pernicious type Not so marked in the infantile form Usually $2\frac{1}{2}$–4 million r b c with corresponding reduction of hæmoglobin

Leucocytes Usually leucopenia

below	3 000 in	95 per cent of cases
	2 000	73
	1 000	42

$\frac{\text{wbc}}{\text{rbc}}$ normal $\frac{1}{750}$ K A $\frac{1}{1\,500}$ or $\frac{1}{2\,000}$ (Diagnostic)

Eosinophiles reduced Relative increase in large mononuclears and lymphocytes Auto-agglutination of r b c (cold agglutinins) common with diminished coagulability diminished alkali reserve euglobulin in serum In terminal stage bilirubinæmia and indirect Van den Bergh reaction +

CLINICAL FEATURES

Incubation period varies—may be as short as ten days—usually unascertainable (Kirk in Sudan 3–6 months) Infection may lie latent *for as long as* $2\frac{1}{2}$ *years (Jopling)* *Onset gradual or sudden* with high fever rigor vomiting Initial fever intermittent with double remissions (double crisis) sweating severe duration 2–6 weeks Waves of fever somewhat resemble undulant daily rigors not uncommon Splenomegaly + hepatomegaly later Slight lymphadenitis common in groins but cervical glands involved in Chinese form Intervals of apyrexia and improvement finally low fever sets in In Kenya special form with primary lesion on legs in goatherd boys at site of infective bite with lymphatic spread to regional glands and eventually to the viscera Rheumatic pains in limbs Amenorrhœa in women Tongue clean appetite good but great emaciation of arms and legs œdema ascites in terminal stages Dusky pigmentation of hands and feet (Black disease) especially in *Europeans* Trophic changes in hair purpura occasional bleeding from gums

Gingivitis and stomatitis common Spontaneous recovery possible Acute and specially resistant cases in Sudan N Kenya and Mediterranean Death may occur in four months Frequent terminal complications bacillary dysentery tuberculosis pneumonia also K A dysentery due to L D bodies in intestines Noma and cancrum oris now considered due to agranulocytosis of which two kinds observed —

1 Due to leishmania infection
2 Due to antimony treatment

Prognosis grave (see treatment)

Infantile K A —Onset insidious splenomegaly anæmia general lymphadenitis Has been confused with Banti s di ease

Dermal leishmanoid —Dermal lesions noted in K A ulceration especially in Sudan (possibly combination of K A and O S but not usually found together)—rare in India Also nodular diffuse papular eruption of face and trunk often in antimony treated patient (post K A leishmaniasis) Lesions usually appear 2–3 years after signs of visceral infection have disappeared **Xanthoma** type orange-coloured plaques which do not ulcerate De pigmented areas of skin frequently encountered on face and upper extremities At first very small they gradually enlarge to irregu lar areas ½ in in diameter Nodules may replace depigmented patches Often confused with leprosy

Pathology Histiocytes and clasmatocytes beneath epidermis con taining parasites not usually in large numbers

DIAGNOSIS

Confused with chronic malaria splenomegaly irregular pyrexia leucopenia from endemic zones suggest K A quinine and other antimalarial drugs ineffective in reducing fever L D bodies demonstrated by spleen liver sternal and lymph gland puncture **Spleen puncture** most satisfactory but may be dangerous Patient in jected with 1/100 gr (0 648 mgm) of atropine and skin anæsthetized Record syringe with dry barrel and No 10 needle Pulp extracted expressed on clean slide and stained with Leishman s stain or Giemsa L D bodies easily seen in splenic pulp cells **Liver puncture** same technique Usual mistake is to take too much blood L D bodies scantier than in spleen **Sternal puncture** with special puncture needle (Witts) L D bodies easily obtained material suitable for culture on N N N medium Even in ab ence of parasites myelogram is distinctive granulocytes 23 erythroblasts 24 hyaline leucocytes 53 (Normally granulocytes four times as numerous as erythroblasts and 3 5 times as numerous as hyaline leucocytes) **Lymph gland puncture** dry sterile hypodermic needle No 16 in erted into inguinal gland steadied by finger and thumb lymph massaged into lumen of needle into which it runs by capillary attraction blown out on to slide and stained but L D bodies not always found

Blood examination —In Assam L D bodies frequently found in large mononuclear cells in blood film thick drop method necessary

Also by centrifuging 5 c c of blood diluted in Locke s solution (sodi chlor 9 gm pot chlor 0 4 gm calc chlor 0 2 gm sodi cit 10 gm aq dest 1 000 c c.) at 750 revolutions L D bodies in sediment

Complement fixation test is performed with antigen prepared from spleen of heavily infected hamster This antigen is still active after being powdered and dried

Blood culture —2 c c. of blood mixed with 1 c c of 6 per cent citrate solution in cool incubator left for two hours sediment inoculated into N N N medium incubated at 22 C

Serum tests —Aldehyde formol gel or serum formalin reaction depends upon excess of euglobulin 1 c c. of clear serum in test tube 3 by ½ in add one drop of 30 per cent formaldehyde shake well place in test tube rack at room temperature Solidification in 3–20 min opacity like white of egg is diagnostic In some cases reaction does not become positive until advanced stage of disease Plasma globulin 4 serum albumin 2 8 (normal 2 5 4)

Antimony test (Chopra) —Precipitation on addition of antimony compound (stiburea) Aldehyde and antimony tests of equal value

DIFFERENTIAL DIAGNOSIS —From chronic malaria (hepatomegaly more evident in K A also often œdema of legs) splenic anæmia Egyptian splenomegaly (*Schistosoma mansoni*) chronic brucellosis (*Br melitensis*) malignant endocarditis leucocythæmia visceral syphilis lymphadenoma tuberculosis of spleen indigenous tropical hepatosplenomegaly (Fawdry) in China Philippines and Japan from *Schistosomiasis japonica*

Indigenous splenomegaly is described in S Yemen—has been found in Aden Protectorate and in the Kavirondo and Wakemba in Uganda and Kenya The degree of anæmia varies within wide limits Zlotnick (1955) has described what appears to be a new protozoan parasite in the leucocytes The illness commences with attacks of fever and rigors every five days

TREATMENT

Antimony compounds *Pentavalent preparations* neostibosan urea stibamine (stiburea carbostibamine) antimosan (Fouadin) amino stiburea solustibosan Probably all of equal value In adults given intravenously by steppage doses on alternate days—0 1 gm (1 5 gr) —0 2 gm (3 gr)—0 3 gm (4 5 gr) total varies from 3–10 gm (46–155 gr) dissolved in 2–6 c c of distilled water (not boiled) Injections to be given slowly

Antimony reaction coughing retching vomiting Overdosage gastro-intestinal disturbance and diarrhœa jaundice arthritic pain especially shoulder pain

In children intramuscular injections 0 1 gm In infantile K A in Italy intravenous injections into jugular vein

Action of antimony on L D bodies uncertain No direct action *in vitro* Some Mediterranean Sudanese and Kenya types resist antimony treatment

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Diamidino stilbene (Stilbamide M & B 744) —Not metallic contains NH_2 group Therapeutic dose 1 mgm per kilo intravenous 8–10 injections on successive days of 45 mgm (0 69 gr) dissolved in 10 c c of distilled water must be freshly prepared otherwise liable to develop toxic properties Injected very slowly to avoid vomiting effects considerable fall in blood pressure, temporary decrease in blood sugar flushing of face burning sensation in chest and abdomen—relieved by adrenaline Full therapeutic effect not seen for 10–14 days then shrinkage of *liver and spleen drop in pyrexia increase in weight increase of* leucocytes Has cured cases resisting antimony

Disadvantages —Neuropathies liable to ensue possibly from action on basal ganglia producing anæsthesia of head and neck In some effects are transitory sometimes permanent Epileptiform seizures may ensue Numbness of lips a feature

Pentamidine now considered safer and more satisfactory in same dosages

Splenectomy together with pentamidine injections has been successfully practised in very resistant ca es

After treatment —Agranulocytosis of K A does not respond to *pentanucleotide but to blood transfusion and injection of* adrenaline anæmia responds to iron therapy Spontaneous cure has been recorded

PROPHYLAXIS

Destruction of K A dogs (reservoir host) effective in Sicily Measures against sandfly (*Phlebotomus*) *e g* removal of thatch on roofs and cementing floors DDT residual spray in particular has proved lethal to sandflies in their haunts

B ORIENTAL SORE

Tropical sore Delhi boil cutaneous leishmaniasis Aleppo boil Specific ulcerating granuloma of skin with intial papule (later ulcer) Parasite *L tropica*

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

S Italy Sicily Algeria Tunis Morocco S Greece and Crete Cyprus Egypt Syria Caucasus Palestine (Jordan Valley) Transjordania Iraq Persia Sudan Arabia N Nigeria India (N W Frontier Quetta) Transcaspia Turkestan S China (Hunan) West Indie South and Central America (usually but not invariably with Es Peru Bolivia Brazil Guianas) Mexico West Indies In tropics at beginning of cool season in subtropics and Mediterranean at end of summer early autumn O S may occur in countries where K A is endemic but has distinct distribution O S in W India K A confined to E coast. In N Africa O S occurs N of Lat 35 K A south Persia and Iraq O S very common K A rare In Central Asia O S and K A occur together O S does not protect against K A or *vice versa* In Iraq children contract O S at 2–3 years of age immunity acquired

CLINICAL FEATURES

Characteristic primary sore—indistinguishable from *oriental sore*—heals Secondary intractable ulceration of nose spreading to lips mouth and pharynx with erosion and obstruction involvement of lymphatic glands and multiple sores over body as well Death from secondary complications e g bronchopneumonia syphilis gangrene Commonly affects ears (*Oreja de chicleros*) Sores affect leg 30 head 11 hand 10 hip 4 elbow 4 trunk 3 knee 3 neck 2 buccal mucosa 2 arm 1 (per cent) Atrophic form characterized by dry mucosa and formation of crusts which block respiration Laryngeal lesions produce hoarseness cough and dyspnœa

TREATMENT

For generalized sores pentavalent antimony (not effective in buccal lesions) Trivalent antimony (Fouadin antimosan) much used intramuscular dose 0 5–5 c c 20–30 injections combined with local antiseptic applications such as sulphonamide paste anthiomaline (see p 197) also recommended Streptomycin and thiazamid are used as adjuvants Atebrin (mepacrine hydrochloride) recently recommended injected into base of sores 5 c c of 10 per cent solution together with 1 tablet (0 1 gm) t d s by mouth for seven days Spontaneous cure sometimes

PROPHYLAXIS

Reports from the State of Rio de Janeiro show that DDT residual sprayings play a great part in the elimination of this disease as the insecticide is lethal to sandflies

AFRICAN TRYPANOSOMIASIS

Acute disease produced by blood protozoan—*Trypanosoma* Characterized by fever adenitis rash and eventually invasion of C N S (sleeping sickness) conveyed by tsetse flies—*Glossina*

Two varieties recognized in man—*T gambiense* and *T rhodesiense* Former transmitted by *G palpalis* *G tachinoides* and latter by *G morsitans*

GEOGRAPHICAL DISTRIBUTION

Corresponds with that of tsetse flies concerned

T gambiense W Africa Gambia Sierra Leone Gold Coast Nigeria Congo S Sudan Uganda In S Africa new focus Ngamiland vector *G palpalis* in Ghana and N Nigeria *Glossina tachinoides*

T rhodesiense Nyasaland N E Rhodesia S E Tanganyika Portuguese E Africa Vector *G morsitans* also occasionally *G swynnertoni* Associated with big game

ÆTIOLOGY

T gambiense and *T rhodesiense* cannot be differentiated by morphology former adapted to man latter principally parasite of antelopes. Status still uncertain

Trypanosome elongated with slender body, pointed anterior end, blunted posterior end, central nucleus, marginal undulating membrane terminating anteriorly in free flagellum; swims with flagellar end foremost. [illegible] near posterior extremity. [illegible] in blood plasma, intercellular tissue spaces, lymph glands, brain.

Development in tsetse: cyclical; [illegible] metacyclic forms [illegible] and in salivary glands. Cycle depends on temperature, usually 18 days. [illegible] conveyed by [illegible] per cent of wild flies (both sexes) infected. [illegible] up to 4th day [illegible]. Direct mechanical transmission [illegible] responsible for some epidemics.

Congenital trypanosomiasis: as in malaria, [illegible] congenital transmission may take place.

Cultivation: on blood media frequently [illegible].

Reservoir hosts: In laboratory [illegible] animals, especially antelopes. In nature [illegible] (*[illegible] spekei*) carrier of *T. gambiense*. Waterbuck ([illegible]), reedbuck (*Cervicapra arundinum*), duiker ([illegible]) and other antelopes normally harbouring *T. rhodesiense*. Wild animals show no signs of disease.

PATHOLOGY

Analogy with *Syphilis*. Changes in C. N. S. and enlargement; hyperplasia of lymphatic glands, proliferation of lymphocytes and reticulum. *T. gambiense* in lymph spaces of connective tissues and glands.

Brain: no gross lesions. Lepto-meningitis; Virchow-Robin space and choroid plexus flattened; fluid extends vertically halfway down; later plexus. Spinal canal may be blocked by cell proliferation.

Blood vessels: infiltration (perivascular cuff); large distended morula cells; Marshalko cells—degenerated plasmocytes. Lumen of vessel contracted; walls thickened.

C.S.F.: increased pressure and proteins; cells 15-500 per c.mm. (lymphocytes, mononuclears, morula cells, eosinophiles and trypanosomes). In advanced cases trypanosomes in brain tissue—frontal lobe, pons, medulla—aggregated into masses without relation to blood vessels. Trypanosomes enter canal from choroidal plexus.

Eyes: interstitial keratitis; optic atrophy occasionally.

Other organs: toxic changes; hæmorrhages and ecchymoses.

T. rhodesiense sleeping sickness: similar, but more acute changes as a rule. Massive effusions into pleural, peritoneal and pericardial cavities, and inflammation of myocardium. Although C.S.F.

CLINICAL FEATURES

Characteristic primary sore—indistinguishable *from oriental sore*—heals Secondary intractable ulceration of nose spreading to lips mouth and pharynx with erosion and obstruction involvement of lymphatic glands and multiple sores over body as well Death from secondary complications *e g* bronchopneumonia syphilis gangrene Commonly affects ears (*Oreja de chicleros*) Sores affect leg 30 head 11 hand 10 hip 4 elbow 4 trunk 3 knee 3 neck 2 buccal mucosa 2 arm 1 (per cent) Atrophic form characterized by dry mucosa and formation of crusts which block respiration Laryngeal lesions produce hoarseness cough and dyspnœa

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ÆTIOLOGY

T gambiense and *T rhodesiense* cannot be differentiated by morph ology former adapted to man latter principally parasite of antelopes Status still uncertain

Trypanosome elongated with slender body pointed anterior end blunted posterior central nucleus marginal undulating membrane terminating anteriorly in flagellum swims with flagellar end foremost Kinetoplast (blepharoplast) posterior to nucleus near posterior extremity Multiplies by binary fission Parasite of blood plasma in terminal stages invades solid organs especially brain

Development in tsetse cyclical in stomach metacyclic forms spreading forward to proboscis and salivary glands Cycle depends on temperature usually 18 days Infection conveyed by bite Eight per cent of wild flies (both sexes) infected *Peritrophic membrane* cylindrical tube suspended in intestine up to 4th day trypanosomes are in lumen of the membrane escape from posterior end passing outside it to proventriculus Direct mechanical transmission by blood on proboscis of Glossina is probably responsible for some epidemics

Congenital trypanosomiasis as in malaria and kala azar congenital transmission may take place

Cultivation on blood media, frequent subinoculation

Reservoir hosts In laboratory domestic and wild animals especially antelopes In nature Speke s antelope (*Limnotragus spekei*) carrier of *T gambiense* waterbuck (*Cobus ellipsiprymnus*) reed buck (*Cervicapra arundinum*) duikerbuck (*Cephalopus grimmi*) and other antelopes normally harbouring *T rhodesiense* Wild animals show no signs of disease

PATHOLOGY

Analogy with *Sp pallida* Chief lesions in C N S and enlargement hyperplasia of lymphatic glands proliferation of lymphocytes and reticulo-endothelium *T gambiense* in lymph spaces of connective tissues and glands

Brain no gross lesions Leptomeningitis in Virchow Robin space and choroid plexus flattening of sulci extends vertically half way down hemispheres Spinal canal may be blocked by cell proliferation

Blood vessels infiltration (perivascular cuff) large distended morula cells Marshalko cells —degenerated plasmocytes Lumen of vessel contracted walls thickened

C S F increased pressure and proteins cells 15–500 per c.mm (lymphocytes mononuclears morula cells eosinophiles and trypanosomes) In advanced cases trypanosomes in brain tissue— frontal lobe pons medulla—aggregated into masses without relation to blood vessels Trypanosomes enter canal from choroidal plexus

Eyes interstitial keratitis optic atrophy occasionally

Other organs toxic changes hæmorrhages and ecchymoses

T rhodesiense sleeping sickness similar but more acute changes as a rule Massive effusions into pleural peritoneal and pericardial cavities and inflammation of myocardium Although C S F

contains numerous trypanosomes brain changes are not so advanced as in chronic *T gambiense* Probably visceral changes are fatal before C N S gets involved

CLINICAL PATHOLOGY

Blood definite anæmia from toxins corresponding diminution in hæmoglobin colour index low auto agglutination of red cells moderate leucopenia (bone marrow) large mononuclears relatively increased increased serum globulin alkali reserve diminished blood sugar low

CLINICAL FEATURES

Incubation period 2–3 weeks Infective bite may cause local reaction

STAGE I *Trypanosome chancre* red discoloured nodule surrounded by œdema Trypanosomes multiply in tissues lesion visible for several months trypanosomes in blood 3 weeks later more numerous during pyrexia Rigor fever like malaria T 99–106° F (37 5–41 C) Hyperæsthesia of periosteum of ulna (Kerandel s sign) Intense temporal headache Tachycardia Enlargement of lymphatic glands—sometimes universal—usually posterior cervical group (Winterbottom s sign) sometimes painful and tender Insomnia lack of concentration fine tremors of lips and hands Splenomegaly usual Local œdemas face (*subocular*) *neck lower abdomen penis*

Rash —Fugitive erythematous macular (like erythema multiforme) usually on chest back upper abdomen may resemble erythema nodosum may be confined to ring on shoulder Brought out by heat (hot bath) Later xeroderma and pruritus neuralgic pain and paræsthesiæ Recurrent orchitis (occasionally) periostitis of tibia (rare)

Eyes —Toxic irido-cyclitis choroiditis optic atrophy (rare)

Death may occur from convulsions status epilepticus coma or intercurrent disease

STAGE II *Sleeping Sickness* (cerebral trypanosomiasis) *Usually* chronic 4–8 months rarely 3 years Sometimes latent period of 7 years may elapse between I and II

Debility languor lack of concentration loss of higher cerebration Slow shuffling gait vacant mask like expression drooping of lower lip Puffiness and drooping of eyelids Stupor somnolence *in day restlessnes at night Dull headache* Animal like habits behaviour often maniacal. Muscular fibrillation tremor *of hands and tongue*

Then bed ridden apathy gross tremors of tongue facial muscles and hands—anorexia torpor deafness Sleeping with unmasticated food in mouth wasting Epileptiform *convulsions with temporary* pareses occasionally meningism Intolerable pruritus of skin bed sores swelling of lips

Finally incontinence coma death

Symptoms sometimes not unlike G P I Reflexes at first exaggerated then absent Urine normal bowels constipated
Clinical categories in natives —
1 Mild—few symptoms—equilibrium between host and parasite
2 Chronic sleeping sickness—commonest
3 Acute—leading to death from toxæmia in some epidemics (in Tanganyika predominates)

Complications and sequelæ—In Europeans recovering from trypanosomiasis cerebration may be temporarily disturbed
In natives complications aggravate and mask disease malaria ancylostomiasis schistosomiasis septic rhinitis otitis media Starvation dysentery and pneumonia frequently terminal

Mortality—Spontaneous recovery often When sleeping sickness stage is well advanced death is inevitable even with modern therapy Whole populations in Central Africa formerly wiped out

Immunity—When disease has lasted long time immunity is acquired (as in wild animals to appropriate trypanosomes) No evidence that immunity in individual is easily acquired Disease more acute in European than in native (usually)

DIAGNOSIS

Blood examination, stained by Leishman examined with low power $\frac{1}{6}$ lens Thick films often useful Centrifuge citrated blood Auto-agglutination of r b c (cold agglutinins) relative leucopenia increase of large mononuclears
Animal inoculation rat or monkey (*Macaca Cercopithecus* best) Blood and lymph culture on appropriate media (Razgha's medium and N N N)

Lymph gland puncture with 16-size hypodermic needle massaging gland (see p 26) Successful in 87 per cent

Sternal puncture recently recommended

Lumbar puncture—C S F for trypanosomes and cell changes

Complement fixation.—Antigen prepared from rats infected with *T equiperdum* injected with ephedrine gives at least 10 per cent more positive diagnoses than any other method

On clinical signs—Differentiation from malaria kala-azar syphilis pellagra leprosy lymphadenoma (Pel Ebstein) In later stages from G P I cerebral tumours encephalitis lethargica cerebral syphilis (N B—Serum of uncomplicated trypanosomiasis may give pseudopositive W R)

TREATMENT

Two main drugs Bayer 205 and tryparsamide

"Bayer 205"—Germanin, antrypol (British), moranyl (French), belganyl (Belgian) Complicated synthetic dye extirpates infection in early stages (blood invasion) Chemotherapeutic index high *i e dosis tolerata* is 160 times *dosis therapeutica* Intravenous injection 1 gm (15 4 gr) in 10 c.c. distilled water Total for cure

10 gm (154 gr) 1 gm on 1st 3rd 10th and 13th days thereafter at weekly intervals *Intramuscular* less satisfactory *intrathecal* contra indicated

TOXIC EFFECTS —Drug cumulative excreted in urine causing albumin and granular casts but no permanent injury May cause toxic dermatitis

Tryparsamide—arsenical—sodium salt of N phenylglycineamide-*p* arsonate Similar preparations tryparsanyl etharsanol proparsanol neocryl mapharsen orsanine (French) Given intramuscularly or intravenously—latter satisfactory Enters cerebrospinal fluid therefore useful in sleeping sickness stage Chemotherapeutic index low (ratio between curative and maximum tolerated dose) 1 2

Large dosage 1–4 gm (15 4–61 6 gr) In average case 1 gm (15 4 gr) in 10 c c distilled water (alkaline) subsequently 2 gm (30 8 gr) three times weekly Total dosage 24 gm (369 6 gr) In chronic cases up to 80 gm (1 232 gr) In advanced cases 0 02 gm per kilo on 4th day 0 03 gm, on 8th day 0 04 gm per kilo —course of 20 injections

TOXIC EFFECTS —Neuritis occasionally (optic neuritis most dangerous) optic atrophy Treatment must be controlled by charting fields of vision (perimeter) Premonitory signs photophobia lachrymation pain

Evidence of cure physical improvement and normal C S F *absence* of albumin and cells

Synergic —Combined treatment now advocated Preliminary injections of antrypol (Bayer 205) 1–3 (1 gm —15 4 gr —each) followed by 12 of tryparsamide (20–24 gm —308–396 6 gr) or alternating treatments (Now used in Belgian Congo Tanganyika Nyasa land Uganda)

Melarsen B (Freidheim)=arsobal (France and Portugal) (B—BAL) 3 6 per cent sol 4 mgm per kg Non toxic in moderate doses By mouth 150 mgm and intravenously 25 mgm Effective in second stage cases in three doses in weekly injections Much used in French and Portuguese West Africa No other drug has produced such good results in advanced *T rhodesiense* cases

Other drugs —4 4 diamidino stilbene (stilbamidine) synthetic non metallic compound causes reduction of blood sugar Tolerated dose 30 times minimum curative dose (see p 28)

Pentamidine isethionate rated superior to stilbamidine Intramuscular *daily injections for 18 days* Doses from 1 6 to 5 15 mg per kg Intravenous 2 mg per kg Injection made slowly Polyneuritis may ensue Pentamidine recommended for mass treatments

PROPHYLAXIS

Tsetse flies—*Glossinae* more than twenty species known confined to Central Africa and S W Arabia—are sombre-coloured insects 6–13 5 mm long somewhat resembling but bigger than *stable flies*

(*Stomoxys*) but with thick proboscis projecting horizontally large wings overlap like scissor blades They are long with the 4th longitudinal vein curved sharply forward to meet short transverse vein at right angles In some species abdomen marked by well-defined brown bands interrupted in mid line In *males* beneath end of abdomen external genitalia form knob like protuberance sexes easily determined Both sexes feed voraciously on blood Proboscis in 3 parts—*labrum hypopharynx labium* *G palpalis* and *G morsitans* active and feed all day from one hour after sunrise onwards One species *G brevipalpis* bites only after dark Glossina bite usually painless but may strike nerve-ending Proboscis plunged to back of bulb then withdrawn a little and sucking proceeds Bulb contains muscles activating cutting mechanism at tip of proboscis

Life history —Pupiparous larvæ mature one at a time within abdomen Egg hatches larva nourished by secretion from milk glands reaches uterus in 10 days Larva deposited by female ½ in into loose soil or sand or beneath leaves or logs Pupa hardens and darkens Pupal stage 3–4 weeks Adult lives 3–6 months produces 6–12 larvæ *G palpalis* *G tachinoides* (smallest) *G morsitans* (most important)

G palpalis —Gambia Niger Benue and Congo rivers at 28° C Constant high humidity and fairly heavy shade necessary not found in dense virgin raw forest. Range varies in different seasons according to food supply Primary foci in dry secondary in rainy seasons Always in vicinity of water Feeds on game birds monitors lizards crocodiles domestic animals man Closely associated with latter Maintained on human blood but can subsist on crocodiles Follows many objects cars bicycles boats Pupates in green places never more than 20 yards from water on dry bank shaded from sun

G tachinoides never closely associated with man Feeds largely on game Puparia in dry sandy soil or shade near water Very important relation to trypanosomiasis especially virulent form in N Nigeria

G swynnertoni is locally distributed in Tanganyika and parts of Kenya and is an important vector for *T rhodesiense* and for trypanosomes of cattle It transmits trypanosomiasis to man at Mwanza L Victorian It is a game feeder

G morsitans conveys trypanosomes of wild game and domestic animals especially *T brucei* of antelopes and *T rhodesiense* (similar to *T brucei*) of man Distribution in W Africa corresponds to *G palpalis* but more extensive In Nyasaland occurs beyond range of latter S limit is Zululand Habits different never flies with *G palpalis* open country more resistant to dry conditions therefore wider range In dry season throughout E Africa in Savannah (bush) country at all seasons but in W Africa is forced back to primary foci in dry season. Feeds largely on man or any living animals particularly associated with game not

10 gm (154 gr) 1 gm on 1st 3rd 10th and 13th days there after at weekly intervals *Intramuscular* less satisfactory *intrathecal* contra indicated

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Evidence of cure physical improvement and normal C S F absence of albumin and cells

Synergic —Combined treatment now advocated Preliminary injec *tions of antrypol (Bayer 205) 1–3 (1 gm —15 4 gr —each) followed* by 12 of tryparsamide (20–24 gm —308–396 6 gr) or alternating treatments (Now used in Belgian Congo Tanganyika Nyasa land Uganda)

Melarsen B *(Freidheim)=arsobal (France and Portugal)* (B=BAL) 3 6 per cent sol 4 mgm per kg Non toxic in moderate doses By mouth 150 mgm and intravenously 25 mgm Effective in *second stage cases in three doses in weekly injections* Much used in French and Portuguese West Africa No other drug has produced such good results in advanced *T rhodesiense* cases

Other drugs —4 4 diamidino stilbene (stilbamidine) *synthetic non* metallic compound causes reduction of blood sugar Tolerated dose 30 times minimum curative dose (see p 28)

Pentamidine isethionate rated superior to stilbamidine Intramuscular *daily injections for 18 days* Doses from 1 6 to 5 15 mg per kg Intravenous 2 mg per kg Injection made slowly Polyneuritis may ensue Pentamidine recommended for mass treatments

PROPHYLAXIS

Tsetse flies—*Glossinae* more than twenty species known *confined to Central Africa and S W Arabia*—are sombre-coloured insects 6–13 5 mm long somewhat resembling but bigger than stable flies

dependent on human blood Concentration varies with distribution of game fly belts therefore variable Puparia in dry friable earth—in E Africa under fallen logs placed so as to catch morning sun (*See* P A Buxton The Natural History of Tsetse Flies 1955)

PROPHYLAXIS OF TRYPANOSOMIASIS

Based on bionomics of tsetse flies Avoidance of fly belts *G palpalis* belt is usually narrow strip of bush on water's edge—range beyond one mile

I MEASURES CONCERNING MAN

Early diagnosis and treatment of infected individuals

Mass injection of natives with arsenicals—tryparsamide (Congo)—lowers index of new infections objection arsenic fastness rapidly acquired by trypanosome and then acquired character transmitted through Glossina (Yorke)

Prevent contact between man and fly by mass movement of infected population to fly free area (as in Sesse Islands of Lake Victoria 50 years ago)

Clear bush along lines of communication round houses ferries wells roads Segregation of big game into game reserves for *G morsitans* Fly follows big game

II MEASURES CONCERNING FLY

(*a*) **Fly itself**—Trapping and catching by hand Training fly boys Fly paper or tanglefoot on clothes and wooden shields on backs of natives or on screens Glossina extirpated on isolated islands *e g* Principe in Bight of Benin Respond to moving objects bicycles or motor cycles and can thus be caught

Fly traps—Harris most effective against Glossina especially *G palpalis* Consists of light canvas trap as big as and roughly resembling cow Full trap 1–200 flies daily especially in Zulu land *not so successful against G morsitans*

(*b*) **Haunts of fly**—Clearing only effective if constantly renewed in bush country causes soil erosion More successful for *G palpalis* than *G morsitans* Form artificial breeding places by piled up logs properly supervised where pupæ are collected and destroyed DDT action on tsetse flies not yet worked out Five per cent solution in kerosene sprayed on screens and on cattle is lethal and deters flies from probing whilst solution leaves behind crystals which are rubbed off but 1 per cent solution in kero ene emulsified with an equal quantity of 5 per cent gum is most effective especially against *G pallidipes morsitans* and *swynnertoni* Spraying of DDT by aeroplanes using finely atomized spray has been proved effective in limited areas in Zululand Twenty per cent solution dissolved in four parts of toluene oil and seven parts of C I fuel oil At speed of 120 m p h aircraft covered 50 acres per mile with swathe width of 70 yards Sprayed 3 times in 5

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weeks allowing for normal gestation period of flies. Total eradication not achieved but reduced to low level. Poison Bait cattle sprayed twice weekly with DDT have been used to reduce numbers of *G. morsitans* and *G. swynnertoni* with success in N. Tanganyika.

Chemoprophylaxis.—Prophylactic injection of "Bayer 205" (antrypol) 1 gm. (15.4 gr.) does not prevent infection but mitigates pathogenicity of trypanosome. Relative protection lasts 3 months. Has been tried extensively in Belgian Congo. Pentamidine prophylaxis also employed—injections 4 mgm. per kg. body weight at intervals of six months. Incidence reduced to $\frac{1}{13}$ of former figure. Antrypol injections combined with this drug inhibit some of the toxic effects.

Antrycide chloride destroys *T. rhodesiense* in doses of 25 mg. per kg. and when injected subcutaneously possesses marked prophylactic properties. It is specially suitable for cattle and other animals which may serve as reservoir hosts.

S. AMERICAN TRYPANOSOMIASIS (CHAGAS' DISEASE)

Acute and chronic, caused by *Trypanosoma cruzi*, disseminated by winged bugs (*Reduviidæ*). Lymphadenitis, splenomegaly.

GEOGRAPHICAL DISTRIBUTION

Brazil, N. Argentine, Panama, Guatemala, Bolivia, Peru, Uruguay, San Salvador, Venezuela, Ecuador, Mexico, Colombia.

ÆTIOLOGY

T. cruzi small, C-shaped, scanty in blood, more abundant in children. Sometimes referred to genus *Schizotrypanum*. Proliferates by schizogony in internal organs and in striated muscle fibres, especially cardiac: rapid multiplication, formation of leishmania nests; later trypanosomes; these invade bloodstream and form broad and slender forms. Easily cultured on blood medium.

Life history.—Development in bug. Trypanosomes ingested by *Panstrongylus megistus* and allied species pass through many stages in intestinal tract; 8–10 days, fully formed *metacyclic* forms reappear in hindgut, pass out through fæces. Infection by defæcation into wound caused by bite. Transmission in bug also hereditary. Development in larval, nymphal or adult stage of insect is so readily observed that method is used for diagnosis (*Xenodiagnosis*). Under natural conditions domestic cat is infected; all laboratory animals susceptible. Congenital transmission may occasionally occur in man.

In Brazil bug is *Panstrongylus megistus* (Barbeiro); in N. Argentine *Triatoma infestans*; in Uruguay *T. rubrovaria*; but other species of *Panstrongylus*, *Rhodnius*, *Eratyrus* and *Triatoma* can also serve.

Chicago) water borne but may be fly borne In tropics commonly (as in China) conveyed by vegetables grown by native cultivators Any age affected most often adults rarer in small children especially Europeans under five but may occur in infants where there is gross lack of sanitation Some races especially susceptible as in the Bantu tribes and in Zulus in Natal where small children are attacked In most countries men are more liable than women House infection insanitary habits promote spread as in Liverpool outbreak (Adams) In Britain and in N Europe generally where the infection is present on a small scale clinical cases of any degree of severity are rare but it has recently been recorded in a high proportion of mentally defective children in the London area

Secondary amœbiasis especially amœbic absces of liver very rare in children

Mnemonic transmission— fæces flies fingers food

ÆTIOLOGY

Entamœba histolytica occurs in three main phases in the intestine submucosa mucosa and fæces

(*a*) **Active or vegetative forms** (trophozoites) generally observed in bloody and mucous fæces Tissue invading form causing ulceration of large intestine clear faintly greenish transparent 20–30 μ in diameter When active ejects hyaline pseudopodia moves like slug at express speed with flowing or gliding movement Outer clear ectoplasm inner granular endoplasm Ingests by pseudopodia r b c leucocytes and tissue particles Fluid absorbed by osmosis Multiplies by binary fission *nucleus* hardly visible in living state, consists of outer beaded chromatin ring with central karyosome (characteristic) In fæces often occurs in clumps or masses Lives only few hours outside the body Movements facilitated by warm stage Degenerated individuals contain vacuoles To see fine points of structure staining methods necessary Small races of *E histolytica* recognized

(*b*) **Precystic forms** derived from tissue invading individuals or from metacystic individuals Active amœbæ divide give rise to smaller individuals which expel all food particles and cease to feed Rounded small (5–20 μ) with sluggish movements cytoplasm devoid of vacuoles and no ingested r b c They are smaller than the lumen (*minuta*) form Precystic amœba rounds up and secretes a thin membrane or cyst wall

(*c*) **Cysts,** round circular in fæces and bowel lumen not in ulcers or metastatic lesions Vary in size some races 7–9 μ others 15–20 μ Nucleus divides by fission into two then four Quadrinucleate cyst characteristic nuclei retain distinctive character Usually contain refractile *chromatoid bodies* and iodine staining glycogen mass sometimes seen in precystic Do not hatch in intestine nor develop further in fæces remain viable 10 days or longer After passing through stomach (cyst wall insoluble in



Plate VI Active *Fntamoela histolytica* some with ingested blood corpuscles in the stools of Amoebic Dysentery Note rouleaux of erythrocytes and charcot Leyden crystals

gastric juice but soluble in trypsin) hatch in intestine of new host into quadrinucleate amœbulæ, which escaping by a small pore divide by mitosis giving rise to eight uninucleated metacystic individuals These feed on bacteria in the lumen of the bowel and are known as lumen or "minuta" forms

Alternative or coprozoic cycle described by Hoare in the symptomless or cyst-carrier state In this the lumen-dwelling amœbæ (*minuta* forms) live on bacteria in the bowel and produce cysts in the fæces

Non pathogenic human amœbæ resembling E histolytica

Entamœba moshkovskii which resembles *E histolytica* in every detail discovered in 1941 in sewage in Russia and confirmed in the U S A England and Brazil is non pathogenic to man and laboratory animals

E invadens a common parasite of snakes is also morphologically identical

Entamœba coli —Inhabitant of intestinal canal of over 50 per cent of normal individuals in tropics often found in fæces of bacillary dysentery and other intestinal diseases normally lives in fæces Not infrequent in temperate climates Individuals on average larger (10–40 μ) with sluggish movements and gradual extension of pseudopodia Cytoplasm bulky granular contains food vacuoles bacteria yeasts occasionally cysts of other amœbæ and intestinal protozoa No differentiation between ecto and endoplasm does not ingest r b c. *Nucleus* large coarse with nuclear ring visible in living state Cysts larger than those of *E histolytica* (10–30 μ) variable in size number of nuclei varies from 1–8, usually 8 Cytoplasm granular contains glycogen Iodine staining glycogen vacuole with sharp outline disappears before 4 nucleated stage is reached Chromatoid bodies occasionally rod like Cultured on same media as *E histolytica* not affected by emetine

E polecki an intestinal amœba of the Rhesus monkey which resembles *E coli* very closely has been reported from man in California

Endolimax nana commonly found in fæces in tropics—almost more frequent than *E coli*—small species (6–12 μ) with granular vacuolated protoplasm containing bacteria or other food material nucleus characteristically vesicular Cysts small very numerous in fæces ovoid or spherical (6 μ) usually contain four nuclei therefore resemble *E histolytica* Nuclei character c iodine-staining glycogen binucleate forms no chromatoid body but sometimes long filamentous rods

Iodamœba butschlii —Non pathogenic parasite of man monkey and pig commonly associated with *E histolytica* Small amœba in fæces (9–10 μ, sometimes 5 μ) characteristic vesicular nucleus with well-defined central karyosome Cysts uninucleated irregular spherical or ovoid (6–16 μ) Refractile volutin granules large dense iodine-staining glycogen mass cyst nucleus excentric and large *I butschlii* amenable to emetine and emetine bismuthous iodide treatment

Dientamœba fragilis—Probably not an amœba but stage in flagellate allied to *Histomonas maleagridis* (blackhead in turkeys) Small (3 5–12 μ) and actively motile with marked differentiation between ecto- and endo-plasm Nucleus has large karyosome composed of granules Lives on bacteria does not produce cysts only survives for short period after passage in stool

Cultivation of E histolytica—From active vegetative forms or from cysts in special media—blood agar or solidified egg slope containing starch granules frequent subculture necessary Symbiosis with bacteria usually *Bact coli* necessary but has been grown in tissue culture and in chicken embryo in absence of bacteria

Reproduction of disease in animals—By intrarectal injection of fæcal material or culture into cats dogs guinea pigs and monkeys Cats (kittens) most susceptible

Cyst carriers (cyst passers)—In endemic areas *E histolytica* cysts commonly found in fæces in absence of symptoms amœbæ ingest bacteria (coprozoic phase) symptomless state may persist or may lead subsequently to intestinal amœbiasis or liver abscess Carriers are healthy individuals without intestinal lesions but should be treated as potential source of infection Carrier rate varies considerably In England although indigenous amœbic dysentery as such is almost unknown carrier rate 2 9–9 7 per cent Egypt 11 5 per cent parts of Holland N Russia and U S A 12 per cent Rate in Iraq India S China and tropics generally much higher probably 20–70 per cent statistics variable Carriers discharge up to 6 000 000 cysts per gm fæces the total output per day ranging from 330 thousand to 45 million

N B—It is important to remember that ulceration of bowel can *exist without symptoms In New Orleans lesions found in 6 per cent* of routine accident autopsies

Contact carriers with healed ulcers no evidence of infection but cysts present produced by *minuta* coprozoic forms

Convalescent carriers—On partial recovery from amœbic dysentery with ulcers still active

PATHOLOGY

In majority of cases infection is limited to lumen of bowel and amœbæ live on surface of mucosa and among bowel contents where they ingest bacteria starch granules and fæcal debris so that bacteria can be demonstrated in amœbæ by staining as in cultural forms Owing to poor diet in human intestine they remain small (*minuta* forms) Possibly majority of cyst passer cases harbour this coprozoic commensal harmless form When bowels are normal and formed stools are passed the cysts in the fæces afford only evidence of amœbic infection but when stools are loose medium sized amœbæ containing ingested bacteria may be passed *E histolytica* inhabiting the gut lumen and producing cysts lives in harmony with host as commensal When some trauma to the mucuous membrane of the bowel is produced

possibly from bacterial infection (Westphal) the host parasite relationship is altered as *E. histolytica* is potentially pathogenic and develops virulent properties manifesting itself by invasion of the intestinal wall. The amoebæ then attach themselves to the mucosa and secrete a cytolysin which destroys the host cells and invade submucosa. This produces local necrosis, abscess formation and a flask-shaped ulcer. Precystic forms are evolved, then cysts which pass into fæces and are voided. Small submucous abscesses form ulcers in long axis of large intestine: cæcum, hepatic flexure, rectum, splenic flexure (mostly cæcum and sigmoid); lower portion of small bowel involved rarely. Blood vessels show engorgement and thrombosis. Intervening mucosa normal. Healing (granulation tissue) leaves slate-coloured parchment scar. Ulcers vary greatly in size; may extend down rectum to anal margin; contain black sloughs (Dyak hair sloughs) or sea-anemone ulcers. Thickening and hypertrophy of bowel wall are seen. There may be also sacculations and cicatricial contractions. Thrombosis of deep blood vessels (amœbæ in thrombi), gangrene of bowel wall and hæmorrhages. Perforation of ulcers may cause peritonitis or localized pericolic abscess; amœbic perforation of appendix recorded. Polypoid or gangrenous destruction of mucosa is terminal due to secondary septic infection. Amœbic granuloma or amœboma resembling carcinoma is not uncommon.

Microscopical.—*E. histolytica* in base of ulcers and submucosa produces gelatinous necrosis due to cytolysins with little surrounding tissue reaction; mostly lymphocytes, mononuclears and plasma cells and few polymorphs unless secondary bacterial invasion is present. Portal pyæmia is due to secondary invasion of liver by entamœbæ from thrombosed veins.

Clinical pathology.—In uncomplicated amœbiasis there is no marked anæmia and a moderate leucocyte increase (10–1[illegible] 000) with low proportion of polymorphs—about 70 per cent.

CLINICAL FEATURES

Incubation period very variable—may be prolonged for years, but in Chicago outbreak 7–77 days. Great majority of cases are chronic with cysts; acute cases with blood and mucus in fæces rarer. May be diarrhœa only—"amœbic diarrhœa." Generally little interference with general health ("walking dysentery"). Periods of exacerbation alternate with periods of quiescence. Onset is usually insidious; pyrexia is rare and usually means secondary infection, but amœbic fever with high temperature recorded. Abdominal pain and tenderness not so severe as in bacillary dysentery, usually localized to cæcum and sigmoid, occasionally transverse colon. May simulate all kinds of intestinal disease. Amœbic *typhlitis* with acute cæcal pain may resemble *appendicitis*, and differentiation often difficult in absence of *E. histolytica* in fæces. Ba enema may help—[illegible] of [illegible] in amœbic typhlitis. *Appendicitis*: tenderness over McBurney's point, pain on rotation of thigh and usually more pronounced leucocytosis. In hyperplastic form (amœboma) palpable tumours in cæcum and

be supplemented with subsequent course of emetine bismuthous iodide Owing to apparent failures of emetine treatment during recent war it has been assumed that amœbæ readily become emetine resistant. This appears to be due to inadequate initial emetine treatment.

2 **Emetine bismuthous iodide** (E B I) given as red powder in hard gelatin capsules or slipules Enteric coated tablets (emplets) tend to pass through intestinal canal undissolved decompose in large intestine where emetine is set free Acts as intestinal irritant and emetic Dose 1–3 gr course of 3 gr (0 18 gm) for 10 days is sufficient Total dosage 19–36 gr (1 2–2 16 gm) Patient must be kept in bed If given at 10 p m no solid food must be taken after 4 30 p m luminal allonal or tinct opii should be given at 9 30 p m There is usually nausea during night and diarrhœa *E histolytica* cysts disappear on third day E B I eradicates greater part of infection but is not always effective in preventing subsequent relapses in long standing infections especially after prolonged previous courses of emetine injections It is best combined with quinoxyl (see below) *Emetine periodide* (E P I) is less irritating than E B I but probably less effective It is indicated in those intolerant to E B I in the same or larger doses *Auremetine* also easily tolerated 1 gr t d s

3 **Quinoxyl (Chiniofon Yatren),** oxy-quinoline sulphonic acid with iodine is best administered in the form of retention enema in 2½–5* per cent solution in 7 oz (207 c c) water to be retained 6–8 hours daily for 10 days heals amœbic lesions in rectum Foot of bed must be raised and a pillow placed under buttocks This treatment is not widely used but is effective in this condition

4 ***Combined treatment** effective especially in chronic cases* Quinoxyl retention enema daily for 10 days E B I 3 gr (0 18 gm) every night for same period Light diet before 6 p m Dietetic restrictions needed in after treatment—especially avoidance of starches Alcohol forbidden for one month Other forms of combined treatment—emetine emetine bismuth iodide and diodoquin

5 **Penicillin injections and sulphonamides** —Amœbic cases with pyrexia are usually due to secondary infection of amœbic ulcers in intestine In these cases injections of penicillin though without action on amœbæ prove most beneficial Many believe emetine and E B I therapy is enhanced by injections of penicillin 1 5 mega units in addition to 20 gm sulphasuccidine daily for 5 days

6 **Antibiotics** —A number of the newer antibiotics have been tried out in treatment In almost every case the first results have been favourable The main forms are aureomycin terramycin (tetracycline) bacitracin and fumagillin There is no doubt that they stop the diarrhœa influence symptoms and vegetative amœbæ and cysts disappear from the stools Opinions vary as to how these results are obtained Although it has been shown that

* 5 per cent. is saturation point.

aureomycin and fumagillin act upon the amœbæ in culture some believe that the action is indirect by destruction of their food bacteria in the fæces Although immediate effects are good they are not lasting so that relapses ensue after a remission of a month It is probable that the most durable effects are produced by the combination of antibiotics with emetine or E B I

Aureomycin (achromycin and erythromycin) by mouth 0·25 gm 4 times daily at 6-hour intervals for 15 days has instantaneous effect upon the symptoms of amœbic dysentery and the ulcers heal rapidly The disappearance of the amœbæ is rapid and dramatic By the 4th day the majority are clear of amœbæ

7 **Other drugs**.—Stovarsol carbarsone (Eli Lilly) arsenical preparations containing 27 per cent arsenic, tablets or pulvules 4 gr (0·25 gm) twice daily for 10 days Milibis (Wia) is a bismuth arsenical in tablets of 0·25 gm three times daily for seven days is widely used in the chronic stages Nivembin is a combination of chloroquine 65 mgm and di iodo hydroxy-quinoline 300 mgm Diodoquin (dihaloquin) contains 63·9 per cent iodine somewhat similar in composition to iodochloroxy quinoline (enterovioform) Valuable in the treatment of chronic amœbic dysentery—especially in symptomless cyst carriers Tablets 3–2 gr by mouth 8 daily for 15 days

Treatment of amœbic hepatitis.—Patient kept strictly in bed Hot applications (antiphlogistine) over liver Liquid diet saline purge Emetine injections—usually 8 gr (0·51 gm) suffices (1 gr for 8 days) Chloroquine (*aralen*) (see p 245) 0·25 gm t d s combined with emetine—concentrated in liver—has specific action on metastatic amœbæ For persistent pain dry cupping Aspiration of liver (hepatic phlebotomy) may prevent development of hepatic abscess (Occasionally amœbic hepatitis is prelude to amœbic abscess)

PROPHYLAXIS

Depends upon efficient sanitation, uncontaminated water supply and measures against houseflies in subtropical countries where they are excessively prevalent Sand filtered water is free from cysts but chlorination is quite ineffective Unboiled water raw vegetables and fruit possibly contaminated by human fæces must be avoided and food handlers examined for *E histolytica* cysts Coolies orderlies and others so infected should not be employed this is especially important in war time Cyst carriers should be treated by E B I and diodoq[illegible] Cysts survive in fæces at room temperature 2 weeks in re[illegible]ration 2 months High temperatures kill them in a short time 1 2500 solution of bichloride of mercury and 2 per cent carbolic or lysol kills in 30 minutes Fæces disinfected by 1 200 aqueous solution of cresol for 15 minutes

Chemoprophylaxis.—Quinoxyl tablets 4 gr (0·25 gm) or diodoquin, taken at night in hyperendemic areas may possibly serve as prophylactic Further experience necessary

[illegible] COMPLICATIONS OF AMŒBIASIS

[illegible] Hepatic Amœbiasis)

[illegible] DISTRIBUTION

[illegible]

[illegible]

[illegible] attack of dysentery [illegible] but always infection with [illegible] of large intestine usually [illegible] men specially [illegible] except in Durban Most [illegible] affected. *E histolytica* [illegible] found in liver pus [illegible] Rarely [illegible]

PATHOLOGY

[illegible] greyish yellow areas in [illegible] break down to form reddish gummy [illegible] wall. *E histolytica* found in [illegible] they disappear At [illegible] secondarily infected with strepto[illegible] and *Salmonella enteritidis* [illegible] whole liver Multiple [illegible] lobe, with miliary small [illegible] parenchyma, causing [illegible] abscess through valve-like [illegible] secondary lung abscess [illegible] also rupture into other viscera (see [illegible] colour streaked with [illegible] resemble badly made custard [illegible] infected then often green and [illegible] cells leucocytes with [illegible] plaques, cholesterol crystals [illegible] *E histolytica* Pus becomes [illegible] walls of cavity thick, resistant fibrous [illegible] collapse and subsequent [illegible] cases without history of amœbiasis

[illegible] divided anatomically between [illegible] on destruction of parenchyma of [illegible] place, often forming palpable [illegible]

CLINICAL FEATURES

[illegible] may be absent. Generally [illegible] hypochondrium. Sub[illegible] sweats, loss of weight [illegible] shoulder pain in considerable pro[illegible] doming and stretch [illegible] to left shoulder from abscess in left [illegible]

lobe Pyrexia progressive hectic most marked at night. Often fullness and bulging of epigastrium or mid axilla. Liver tender enlarged—usually downwards Hepatic pain relieved by lying on affected side Dullness at base of right lung may be due to compression pneumonia by enlarged liver or secondary involvement of lung and pleura Often pleural effusion (ægophony) and pleuritic rub Amœbæ and pus cells present in effusion Blood rarely no change usually leucocytosis 15–35 000 (polymorphs rarely above 80 per cent.) and severe secondary anæmia rarely of pernicious type Death from toxæmia, cholæmia, rupture of abscess septicæmia

Varieties—May be acute complete destruction of liver tissue and rapid death, or chronic palpable obvious tumour in epigastrium mid axilla or base of scapula spontaneous rupture Marked rigors rare Enlarged cervical axillary and supraclavicular glands not uncommon Dysphagia pain on swallowing when bolus traverses lower end of œsophagus Localized pain on pressure in intercostal spaces is valuable sign Cough, due to reflex irritation of diaphragm Local œdema of chest wall and bulging may indicate site of abscess Jaundice uncommon may be due to toxæmia from secondarily infected abscess or from obstruction of biliary ducts

Rupture into bronchus hæmoptysis and severe cough prune-juice sputum often clubbed fingers likely in chronic cases to be mistaken for tuberculosis Melæna may occur Rupture into pleura (with pneumothorax) pericardium peritoneum, stomach colon through skin of abdominal wall or axilla (amœbiasis of skin may result) or into common bile duct (bilious fistula)

Mortality—Formerly high 50 per cent due in part probably to operative measures then in use Now minimal with better diagnosis and treatment by aspiration combined with emetine injections and chloroquine (*aralen*)

DIAGNOSIS

Not always easy

Common mistakes (1) Failure to diagnose hepatic disease (2) mis-interpretation of basal pneumonia as secondary to intrahepatic suppuration (3) attributing pyrexia to some other fever (malaria) (4) mis-diagnosis of other intrahepatic disease as liver abscess—*e g* suppurating hydatid gumma pylephlebitis gall stones cholecystitis subphrenic abscess appendix abscess localized abscess of abdominal or thoracic wall abscess of liver associated with diverticulitis duodenal ulcer and rarely with ascaris infection melioidosis pleurisy encysted empyema pyelitis schistosomiasis (*S mansoni* and *S japonicum*) ulcerative endocarditis kala azar malignant disease of the liver non parasitic cyst Differential diagnosis from suppurative cholecystitis in absence of X ray examination particularly difficult

Diagnostic Rules.

(1) Suspect liver abscess in all cases of progressive ill health associated with abdominal signs and pyrexia, particularly if accompanied by sweats pyrexia and leucocytosis.

(2) Low grade pneumonia at base of right lung suggests intrahepatic suppuration

(3) Fæces examination *E histolytica* cysts found in 45–50 per cent by concentration methods

(4) X ray examination and screening of excursions of diaphragm shows limitation or fixation of movement paradoxical movement doming tenting or peaking and sometimes altera tion of cardio-phrenic angle to right angle Abscess in centre of liver may be visible especially when margins are cretified Fluid level can be visualized by injection of air or lipiodol

(5) Blood examination leucocytosis usual

(6) Diagnostic aspiration needle inserted at point where abscess lies closest to surface performs up and down pendulum movements with respirations on entering cavity Withdrawal of pus and examination

TREATMENT

(1) **Method of election.**—Emetine injections in pre suppurative stages up to 12 gr (0 76 gm) produce reduction in size of liver abolition of fever and pain Chloroquine (0 25 gm t d s for 7 days thereafter 0 25 gm b d for 10 days maintenance dose 0 25 gm daily) is concentrated in liver appears to be specific for hepatic amœbiasis Nivaquine (chloroquine sulphate) equally effective Antibiotics—aureo mycin and terramycin (oxytetra cycline) much used but not permanently effective unless combined with emetine Afford protection against secondary infection

After treatment with E B I to clear out intestinal infection and to prevent recurrence (combined treatment p 48)

(2) **Aspiration**—If much pus has formed aspirate with Potain s aspirator draw off 20 oz (591 c c) or more pus may re accumulate repeat aspiration and continue with emetine treatment and chloroquine If pus is too viscid inject eusol (equal parts with saline) into abscess cavity If secondarily infected with bacteria inject penicillin—mega unit—into abscess cavity

Rules—Never aspirate with Potain s aspirator unless all preparations are made for open operation and electric sucker is at hand Gas and oxygen anæsthesia The spot to be selected is indicated by physical signs preferably between 8th and 9th intercostal spaces well below line of pleura in anterior axillary line 1½ in along costal margin Insert needle upwards inwards backwards for not more than 3½ in (distance of *inferior vena cava* from any part of chest wall is 4 in) Needle swings when liver is entered push it gently forwards until sense of resistance shows that it is in abscess cavity affix syringe and aspirate If costo-phrenic sinus is crossed and there are adhesions pus is indicated

Indications for open operation

(1) When after repeated aspirations no pus is obtained but indications of its presence are too strong to be ignored (May be multiple small abscesses)

(2) When abscess points in epigastrium indicating left lobe abscess. Care must be taken to avoid colon and duodenum

(3) Where large amount of pus is present is secondarily infected and has not yielded to aspiration

Technique of open operation.

Abdominal route—Kocher's subcostal incision Pack off wound edges Insert wide bore sucker straight into liver to prevent extravasation Insert finger into cavity break down loculi Suck out all pus Stitch edge of cavity to parietal peritoneum Insert wide drainage tube (Tudor Edward's empyema tube drain) push to bottom of cavity

Transpleural route—Clear and resect 1½ in of 8th and 9th ribs in posterior axillary line Stitch diaphragm to thoracic wall may be difficult on account of fragmentation of diaphragm

Simpler method—Expose ribs denude of tissues insert iodine gauze pack beneath ribs leave 3-4 days Adhesions form in costophrenic sinus Ribs resected and infection of pleural cavity prevented Insert sinus forceps and use aspirator Insert wide bore tube to ensure free drainage No shortening of tube but let cavity extrude it automatically maintaining it *in situ* as long as there is free drainage Irrigate with Dakin's solution which has solvent action on wall of liver abscess

Prognosis good in most cases If condition is cured and underlying amœbic infection eliminated there is no bar to return to tropics.

Treatment of abscess rupturing into lung—When emetine does not influence fever or diminish symptoms and signs then operative measures must be undertaken especially if amount of expectorated pus increases and patient loses weight. Ribs are resected Lung explored and drained as for abscess. May also be necessary to explore liver but abscess cavity may be collapsed with opposed walls Aspiration preferable to open operation

Rupture into pleura operation as for empyema into peritoneum then laparotomy and drainage Into pericardium open and drain if possible but aspiration repeated may suffice

PULMONARY AMŒBIASIS

Solitary or multiple amœbic abscesses of lung Solitary abscess if not amenable to emetine treatment must be operated as for lung abscess If multiple response to emetine is usually striking Marked pyrexia signs of bronchopneumonic consolidation marked leucocytosis. X ray may assist diagnosis.

AMŒBIC ABSCESS OF BRAIN

Excessively rare may respond to emetine but generally fatal usually secondary to hepatic abscess

be supplemented with subsequent course of emetine bismuthous iodide Owing to apparent failures of emetine treatment during recent war it has been assumed that amœbæ readily become emetine resistant. This appears to be due to inadequate initial emetine treatment

2 **Emetine bismuthous iodide (E B I)** given as red powder in hard gelatin capsules or slipules Enteric coated tablets (emplets) tend to pass through intestinal canal undissolved decompose in large intestine where emetine is set free Acts as intestinal irritant and emetic Dose 1–3 gr course of 3 gr (0 18 gm) for 10 days is sufficient Total dosage 19–36 gr (1 2–2 16 gm) Patient must be kept in bed If given at 10 p m no solid food must be taken after 4 30 p m luminal allonal or tinct opii should be given at 9 30 p m There is usually nausea during night and diarrhœa *E histolytica* cysts disappear on third day E B I eradicates greater part of infection but is not always effective in preventing subsequent relapses in long standing infections especially after prolonged previous courses of emetine injections It is best combined with quinoxyl (see below) *Emetine periodide* (E P I) is less irritating than E B I but probably less effective It is indicated in those intolerant to E B I in the same or larger doses *Auremetine* also easily tolerated 1 gr t d s

3 **Quinoxyl (Chiniofon Yatren),** oxy-quinoline sulphonic acid with iodine is best administered in the form of retention enema in 2½–5* per cent solution in 7 oz (207 c c) water to be retained 6–8 hours daily for 10 days, heals amœbic lesions in rectum Foot of bed must be raised and a pillow placed under buttocks This treatment is not widely used but is effective in this condition

4 **Combined treatment** effective especially in chronic cases Quinoxyl retention enema daily for 10 days E B I 3 gr (0 18 gm) every night for same period Light diet before 6 p m Dietetic restrictions needed in after treatment—especially avoidance of starches Alcohol forbidden for one month Other forms of combined treatment—emetine emetine bismuth iodide and diodoquin

5 **Penicillin injections and sulphonamides** —Amœbic cases with pyrexia are usually due to secondary infection of amœbic ulcers in intestine In these cases injections of penicillin though without action on amœbæ prove most beneficial Many believe emetine and E B I therapy is enhanced by injections of penicillin 1 5 mega units in addition to 20 gm. sulphasuccidine daily for 5 days

6 **Antibiotics** —A number of the newer antibiotics have been tried out in treatment In almost every case the first results have been favourable The main forms are aureomycin terramycin (tetracycline) bacitracin and fumagillin There is no doubt that they stop the diarrhœa influence symptoms and vegetative amœbæ and cysts disappear from the stools Opinions vary as to how these results are obtained Although it has been shown that

*5 per cent. is saturation point

aureomycin and fumagillin act upon the amœbæ in culture some believe that the action is indirect by destruction of their food bacteria in the fæces Although immediate effects are good they are not lasting so that relapses ensue after a remission of a month It is probable that the most durable effects are produced by the combination of antibiotics with emetine or E B I

Aureomycin (achromycin and erythromycin) by mouth 0 25 gm 4 times daily at 6-hour intervals for 15 days has instantaneous effect upon the symptoms of amœbic dysentery and the ulcers heal rapidly The disappearance of the amœbæ is rapid and dramatic By the 4th day the majority are clear of amœbæ

7 **Other drugs**.—Stovarsol carbarsone (Eli Lilly) arsenical preparations containing 27 per cent arsenic tablets or pulvules 4 gr (0 25 gm) twice daily for 10 days Milibis (Win) is a bismuth arsenical in tablets of 0 25 gm three times daily for seven days is widely used in the chronic stages Nivembin is a combination of chloroquine 65 mgm and di iodo hydroxy-quinoline 300 mgm Diodoquin (dihaloquin) contains 63 9 per cent iodine somewhat similar in composition to iodochloroxy quinoline (enterovioform) Valuable in the treatment of chronic amœbic dysentery—especially in symptomless cyst carriers Tablets 3 2 gr by mouth 8 daily for 15 days

Treatment of amœbic hepatitis.—Patient kept strictly in bed Hot applications (antiphlogistine) over liver Liquid diet saline purge Emetine injections—usually 8 gr (0 51 gm) suffices (1 gr for 8 days) Chloroquine (*aralen*) (see p 245) 0 25 gm t d s combined with emetine—concentrated in liver—has specific action on metastatic amœbæ For persistent pain dry cupping Aspiration of liver (hepatic phlebotomy) may prevent development of hepatic abscess (Occasionally amœbic hepatitis is prelude to amœbic abscess)

PROPHYLAXIS

Depends upon efficient sanitation uncontaminated water supply and measures against houseflies in subtropical countries where they are excessively prevalent Sand filtered water is free from cysts but chlorination is quite ineffective Unboiled water raw vegetables and fruit possibly contaminated by human fæces must be avoided and food handlers examined for *E histolytica* cysts Coolies orderlies and others so infected should not be employed this is especially important in war time Cyst carriers should be treated by E B I and diodoquin Cysts survive in fæces at room temperature 2 weeks in refrigeration 2 months High temperatures kill them in a short time 1 2500 solution of bichloride of mercury and 1 per cent carbolic or lysol kills in 30 minutes Fæces disinfected by 1 200 aqueous solution of cresol for 15 minutes

Chemoprophylaxis.—Quinoxyl tablets 4 gr (0 25 gm) or diodoquin, taken at night in hyperendemic areas may possibly serve as prophylactic Further experience necessary

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SECONDARY AMŒBIASIS COMPLICATIONS OF AMŒBIASIS

HEPATIC ABSCESS (Liver abscess Hepatic Amœbiasis)

GEOGRAPHICAL DISTRIBUTION

Corresponds with that of amœbic dysentery

ÆTIOLOGY

Relationship to amœbic dysentery undoubted attack of dysentery may antedate onset by 20 years or longer but always infection with *E histolytica* cysts or cryptic ulceration of large intestine usually cæcum More common in Europeans than natives men specially affected women rarely children hardly ever except in Durban Most common age 20–40 Right lobe of liver usually affected *E histolytica* active vegetative form found in liver pus cysts never Rarely associated with amœbic pericarditis

PATHOLOGY

At first solitary or multiple gummatous greyish yellow areas in centre of liver which afterwards break down to form reddish gummy pus in ragged cavity without limiting wall. *E histolytica* found in numbers at margin of abscess in liquefied pus they disappear At first sterile it later may become secondarily infected with streptococci or other organisms *B (Escherichia) coli* and *Salmonella enteritidis* Single abscess may be large and occupy almost whole liver *Multiple may be five or more size of filbert in one lobe* with miliary small abscesses scattered throughout *surrounding parenchyma* causing intense hyperæmia Rupture of liver abscess through valve-like aperture in diaphragm is not uncommon secondary lung abscess *forms in base of right lung* may also rupture into other viscera (see p 53) Liver pus characteristic chocolate colour streaked with mucus often thick and viscid may resemble badly made custard *odourless except when secondarily infected then often green and* offensive Contains pigmented spherical cells leucocytes with glycogen granules oil globules lecithin plaques cholesterol crystals Charcot Leyden crystals and occasionally *E histolytica* Pus becomes inspissated and absorbed and walls of cavity thick resistant fibrous even cretified Calcification may prevent collapse and subsequent healing Encountered often in cases without history of amœbiasis

Bilaterality of liver—Portal stream divided anatomically between right and left lobe *Therefore on destruction of parenchyma of* right lobe hypertrophy of left takes place often forming palpable tumour in left hypochondrium

CLINICAL FEATURES

Great variety of symptoms subjective may be absent Generally fullness weight and stabbing pain in right hypochondrium Sub icteric look furred tongue pyrexia night sweats loss of weight rheumatic pains at night Right shoulder pain in considerable proportion—reflex irritation of phrenic nerve through doming and stretching of diaphragm Pain referred to left shoulder from abscess in left

(2) Low grade pneumonia at base of right lung suggests intrahepatic suppuration

(3) Fæces examination *E histolytica* cysts found in 45–50 per cent by concentration methods

(4) X ray examination and screening of excursions of diaphragm shows limitation or fixation of movement paradoxical move ment doming tenting or peaking and sometimes altera tion of cardio-phrenic angle to right angle Abscess in centre of liver may be visible especially when margins are cretified. Fluid level can be visualized by injection of air or lipiodol

(5) Blood examination leucocytosis usual.

(6) Diagnostic aspiration needle inserted at point where abscess lies closest to surface performs up and down pendulum move-ments with respirations on entering cavity Withdrawal of pus and examination

TREATMENT

(1) **Method of election.**—Emetine injections in pre suppurative stages up to 12 gr (0 76 gm.) produce reduction in size of liver abolition of fever and pain Chloroquine (0 25 gm t d s for 7 days thereafter 0 25 gm b d for 10 days maintenance dose 0 25 gm daily) is concentrated in liver appears to be specific for hepatic amœbiasis Nivaquine (chloroquine sulphate) equally effective Antibiotics—aureo-mycin and terramycin (oxytetra-cycline) much used but not permanently effective unless combined with emetine Afford protection against secondary infection

After treatment with E B I to clear out intestinal infection and to prevent recurrence (combined treatment p 48)

(2) **Aspiration.**—If much pus has formed aspirate with Potain s aspirator draw off 20 oz (591 c c) or more pus may re accumulate repeat aspiration and continue with emetine treatment and chloroquine If pus is too viscid inject eusol (equal parts with saline) into abscess cavity If secondarily infected with bacteria inject penicillin—mega unit—into abscess cavity

Rules—Never aspirate with Potain s aspirator unless all preparations are made for open operation and electric sucker is at hand. Gas and oxygen anæsthesia The spot to be selected is indicated by physical signs preferably between 8th and 9th intercostal spaces well below line of pleura in anterior axillary line 1½ in along costal margin Insert needle upwards inwards backwards for not more than 3½ in (distance of *inferior vena cava* from any part of chest wall is 4 in) Needle swings when liver is entered push it gently forwards until sense of resistance shows that it is in abscess cavity affix syringe and aspirate If costo-phrenic sinus is crossed and there are adhesions pus is indicated

Indications for open operation

(1) When after repeated aspirations no pus is obtained but indications of its presence are too strong to be ignored (May be multiple small abscesses)

(2) When abscess points in epigastrium indicating left lobe abscess Care must be taken to avoid colon and duodenum

(3) Where large amount of pus is present is secondarily infected and has not yielded to aspiration

Technique of open operation.

Abdominal route —Kocher s subcostal incision Pack off wound edges Insert wide bore sucker straight into liver to prevent extravasation Insert finger into cavity break down loculi Suck out all pus Stitch edge of cavity to parietal peritoneum Insert wide drainage tube (Tudor Edward s empyema tube drain) push to bottom of cavity

Transpleural route —Clear and resect 1½ in of 8th and 9th ribs in posterior axillary line Stitch diaphragm to thoracic wall may be difficult on account of fragmentation of diaphragm.

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Solitary or multiple amœbic abscesses of lung Solitary abscess if not amenable to emetine treatment must be operated as for lung abscess If multiple response to emetine is usually striking Marked pyrexia signs of bronchopneumonic consolidation marked leucocytosis X ray may assist diagnosis.

AMŒBIC ABSCESS OF BRAIN

Excessively rare may respond to emetine but usually secondary to hepatic abscess.

AMŒBIC ABSCESS OF SPLEEN PERICARDIUM EPIDIDYMIS AND VAGINA

Splenic abscess excessively rare associated with hepatic abscess Amœbic pericarditis may be primary but usually secondary to hepatic abscess Treated on surgical lines Rarely genito urinary amœbiasis may be associated with presence of *E histolytica* in the urine Amœbic ulceration of vagina reported from India

AMŒBIC INFECTION OF SKIN

May be secondary to ruptured liver abscess and associated with rib necrosis or of abdominal wall secondary to operations on bowel, such as colostomy or opening of perirectal abscess Massive gangrene of abdominal parieties much dark evil smelling anchovy-sauce pus containing active amœbæ Response to emetine injections remarkably effective and rapid Perirectal abscess may rupture and spread to skin of buttocks and back, causing great tissue destruction May occur in patients with *E histolytica* cysts in fæces in absence of dysenteric symptoms

BALANTIDIASIS

Infection of large intestine with ciliate protozoan *Balantidium coli* producing symptoms and pathology resembling amœbic dysentery

Geographical Distribution.—*Balantidium* is normally a parasite of pigs and causes fatal disease in chimpanzees in captivity In man found in Russia Scandinavia Siberia Georgia Finland Germany Austria Holland China Andaman and Sandwich Islands Egypt Sudan N America Brazil Porto Rico and England

Ætiology—*Bal coli* is a large oval ciliated protozoan (30–200 μ by 40–60 μ) clothed with cilia with a kidney shaped macronucleus and approximated micronucleus food vacuoles anterior *peristome* and posterior *cytophage* (anus) showing nutrition ingestion of particles Reproduction is asexual by transverse fission but conjugation takes place Cysts are ovoid (50–70 μ) with no cilia passed in fæces It is cultured on the same media as *E histolytica* frequent subinoculations being necessary

Pathology—Resembles amœbic dysentery closely parasite found in submucosa muscular coats blood vessels lymphatics and in mesenteric glands

Clinical Features—Symptoms closely resemble those of amœbic dysentery usually chronic and diarrhœic No specific blood changes

Diagnosis—By fæces examination—balantidia scanty but may be in clumps

Treatment—None satisfactory Carbon tetrachloride 1 dr (3 69 c c) recommended also *carobinase* watery extract of *Jacaranda decurrens* 25 gm (365 gr) in 500 c c of hot water with daily rectal lavage for 3 weeks *Acranil* hydrochlorate of acridine recommended in Germany intramuscular injections of gr ¼ biniodide of mercury said to be specific *In vitro* 1 100 000 solution kills balantidia instantaneously

GIARDIASIS

Infection of small intestine and duodenum with *Giardia* (*Lamblia*) *intestinalis*

Geographical Distribution.—World wide extremely common in tropics In temperate zones especially in children

Ætiology—*Giardia intestinalis* shape of half pear split longitudinally —12–18 μ by 6 μ On ventral surface is concave sucking disc and tail terminates in two flagella Four pairs of anterior flagella arise from blepharoplasts two axostyles with two oval nuclei Multiplies by binary fission Cysts in large numbers bi and quadri nucleate (14 μ) Cytoplasm transparent axostyles and other structures seen Stains well with iodine Cannot be cultured on media.

Pathology—Pathogenicity doubted by some Generally considered irritant parasite attaches itself by sucking disc to villi and invades biliary tract Also found in duodenal and gastric juices ulceration of small intestine described

Clinical Features—May be none In children especially and under war conditions recurrent diarrhœa abdominal discomfort. Fæces fluid and mucoid may be greenish or light-coloured sometimes resembling sprue Cholecystitis (doubtful) and steatorrhœa described Flatulence + Relapses frequent quiescent periods tolerance acquired Fæces may contain cysts in enormous numbers

Treatment—Difficulty in claiming permanent cure on account of latency Atebrin (Mepacrine hydrochloride) specific for active stage and for cysts Dosage 1½ gr (0 1 gm) t.d s for 7 days Now abundantly confirmed Restrict carbohydrates Mainly protein diet *Acranil* recommended by German and Scandinavian authorities in doses from 0 25 gm daily for children under two to 1 5 gm daily for 5 days in those over ten Synthetic anti malarial drugs—chloroquine camoquin (amodiaquin) and azacrin —are also useful in clearing out cysts

FLAGELLATE DIARRHŒA

Designation not strictly correct presence of flagellates in large numbers probably due to liquid intestinal contents. Small flagellates are extremely common in post-dysenteric diarrhœas and also in dysenteric stools Though probably non pathogenic to man, allied species cause intestinal ulceration in laboratory animals notably guinea pigs

Trichomonas hominis pear shaped body (10–15 μ by 7 μ) spherical nucleus at anterior end three long flagella directed forwards and a thicker fourth backwards forms border of undulating membrane and free flagellum small anterior aperture (cytostome) central skeletal rod (axostyle) vacuolated cytoplasm containing food granules No cysts

PLATE VII

HUMAN INTESTINAL PROTOZOA

(Mostly iodine stained preparations)

Entamœba histolytica

1.—Active vegetative form as seen in fresh fæces

2.—Precystic form

3.—Uninucleated cyst

4.—Quadrinucleated cyst with glycogen masses and chromidial bars

5.—Quadrinucleated cyst—small race

Entamœba coli

6.—Active vegetative form in fresh fæces

7.—Precystic form

8.—Binucleated cyst

9.—Octonucleated cyst with chromidial bars

Endolimax nana

10.—Active vegetative form in fresh fæces

11.—Precystic form

12.—Uninucleated cyst.

13.—Quadrinucleated cyst

Iodamœba butschlii

14.—Active vegetative form in fæces

15.—Mature cyst with one nucleus and iodine staining vacuole.

Giardia intestinalis

16.—Active form in fæces

17.—Binucleated cyst

18.—Quadrinucleated cyst (end-on view)

Chilomastix mesnili

19.—Active form in fæces

20.—Mature cyst

Trichomonas hominis

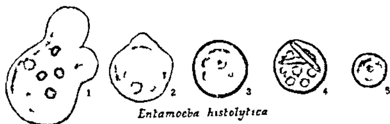
21.—Active form in fæces (no cysts known)

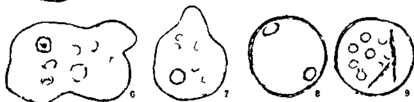
Blastocystis hominis (yeast like organism)

22.—Various forms in fæces

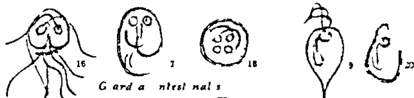
Balantidium coli

23.—Active form in fæces















P man Intestinal Protozoa.

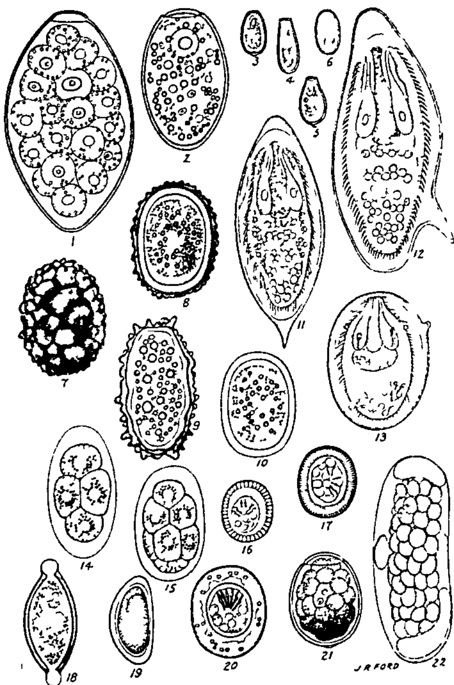


Plate VIII Eggs of the Commoner Helminths found in man

PLATE VIII

EGGS OF THE COMMONER HELMINTHS FOUND IN MAN × 400

1 —*Fasciolopsis buski*
2 —*Paragonimus ringeri*
3 —*Heterophyes heterophyes*
4 —*Opisthorchis felineus*
5 —*Clonorchis sinensis*
6 —*Metagonimus yokogawai* (Yokogawa's fluke)
7 — *Ascaris lumbricoides* (external aspect)
8 —
9 — (unfertilized egg)
10 — (decorticated egg)
11 —*Schistosoma hæmatobium*
12 — *mansoni*
13 — *japonicum*
14 —*Ancylostoma duodenale*
15 —*Trichostrongylus colubriformis*
16 —*Tænia solium*
17 — *saginata*
18 —*Trichuris trichiura*
19 —*Enterobius vermicularis*
20 —*Hymenolepis nana*
21 —*Diphyllobothrium latum*
22 —*Heterodera radicicola* (non parasitic ingested with root vegetables)

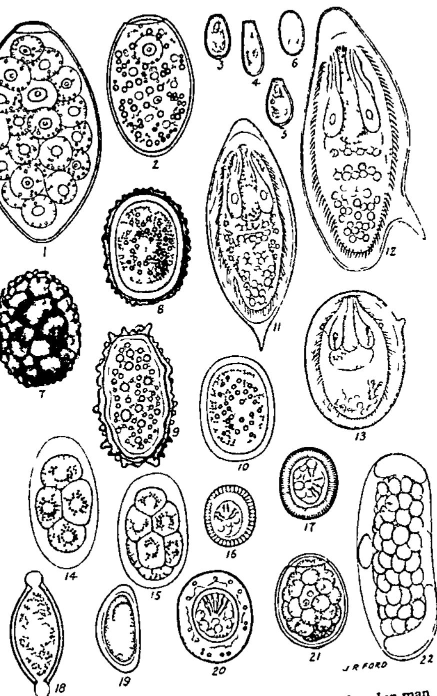


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CLINICAL FEATURES

1 USUAL TYPE —Louse borne form (*Sp recurrentis*)

Course and severity vary greatly in single outbreak Incubation period 2–10 days Often complicates typhus

Onset sudden rigor epistaxis vomiting photophobia headache + T 104° F (may be higher) pulse 110–130 Delirium Skin dry burning icteric tint Spleen enlarged tender Tongue dry furred Abdominal pain muscular pains in legs *Herpes labialis* Occasionally erythematous rash rose-coloured macules or petechiæ in lateral distribution on neck, shoulders chest and abdomen

Primary remittent fever 5–7 days evening temperature highest increased pyrexia on 4th 5th or 6th day with delirium Crisis profuse diaphoresis and diarrhœa sudden drop of temperature to subnormal collapse shrinkage of spleen

Initial fever = first *paroxysm* followed by first apyrexia first relapse second apyrexia and so on Relapses may be more severe but as disease progresses become milder Usually five but number varies in different types *Polyuria before* crisis then diminution of urine Leucocytosis 15–13 000 Polymorphs 80 per cent or over especially during pyrexia Bilirubinæmia in pre critical period indirect Van den Bergh reaction +

Anomalous types—In Abyssinia (1940) dyspnœa hepatitis and diarrhœa Pyrexia may be frankly intermittent with longer periods of apyrexia (17–42 days) Arthritis may supervene Convalescence protracted with nephritis conjunctivitis iritis otorrhœa polyarthritis pneumonia neuritis parotitis adenitis and abortion Abdominal pain may resemble appendicitis

Severe type—Bilious typhoid of Griesinger with hæmatemesis intense icterus splenomegaly purpuric hæmorrhages and albuminuria apt to be mistaken for yellow fever (*q v*) as in Senegal in 1921 Stupor tympanites and hiccough Usually seen in war time

2 CENTRAL AFRICAN TYPE (Carapata disease tick fever) — *Sp duttoni* more severe as a rule Initial fever usually shorter— 3 days Diarrhœa and gastro-intestinal disturbances common Apyrexial periods irregular Five or six relapses the rule may be eleven Fever though shorter is as severe in relapses as in initial paroxysm Rarely fever takes low chronic form with severe head ache and vomiting Iritis is common complication as well as sequela Liver and spleen enlarged *Bronchitis and pneumonia* frequent Parasites in peripheral blood usually scanty Poly morphonuclear leucocytosis and usually a moderate aplastic anæmia

Fulminating cases observed in European soldiers in E Africa spirochætes in large numbers death in 24 *hours* with toxæmia and intense icterus due to impaction of masses of spirochætes in liver and cerebral capillaries In natives much *less severe due to* partial immunity

Neurotropic.—Characteristic feature of *Sp duttoni* infection is neurotropic tendency due to invasion of C N S In recent work in Tanganyika no spirochætes were found in C S F but injection of it into mice produced infection Signs of meningitis observed C S F under pressure and contains excess of lymphocytes Optic atrophy is a serious feature and may accompany the fever or follow after lapse of months Aphasia seen and also destruction of nuclei of cranial nerves 3rd 4th 5th (ptosis strabismus trigeminal neuralgia) 7th (facial paralysis) 8th (deafness)

3 PERSIAN TYPE (mianeh disease)—*Sp sogdianum* or *persica* Syria N Palestine Persia intermediate between 1 and 2 relapses numerous and short spirochætes in blood scanty Temperature may come down by lysis Relapses may last 1–3 days Occasionally severe with jaundice

4 SPANISH TYPE (*Sp hispanica*)—Incubation period 1–2 days Nausea headache congestion of face and eyes herpes labialis common Periods of apyrexia and relapse correspond to 2 usually four relapses Lymphadenitis and nerve complications noted

5 CENTRAL S AMERICAN AND CALIFORNIAN TYPES— More or less resemble 2 Mortality usually below 6 per cent More severe in aged and young or when complicated by other disease as typhus

DIAGNOSIS

On character of fever leucocytosis splenomegaly icterus and presence of spirochætes in blood in pre-critical period W R and Kahn positive in pyrexial and apyrexial period in 20 per cent (pseudo-positive reaction)

Differential diagnosis—From leptospirosis (Weil s disease) typhoid typhus influenza dengue and in W Africa from yellow fever Infarction of the spleen simulates an acute abdomen

TREATMENT

Nursing and dieting important especially after crisis

Salvarsan and neosalvarsan (0 3–0 9 gm 4 6–13 8 gr) intravenously destroy spirochætes and provoke artificial crisis Novarsenobillon and neosalvarsan best Should be given in pre-critical period when temperature is rising not when temperature is falling or in apyrexia or relapses will en ue If salvarsan compounds are injected when crisis is imminent grave toxæmia is precipitated Albuminuria is no contra indication to salvarsan treatment

Arsant (salvarsan compound in which two arsenic atoms are replaced by antimony) recently recommended

Arsenic-fastness rapidly acquired by spirochætes

Collapse and fall of blood pre sure with subnormal temperature following crisis counteracted by strychnine intrarectal salines injections of adrenaline and ephedrine

Penicillin specific Initial dose 1 5 mega units 40 000 every three hours for 60 doses Now recommended in combination with salvarsan

Terramycin (oxytetracycline) by mouth or by intravenous route (0 5 gm daily for 5 days) recommended especially in infections with *Sp persica* resistant to penicillin and arsenical compounds

Prophylaxis—In louse-conveyed form anti louse measures on approved lines In tick borne forms measures based on habits of *Ornithodorus* In Central Africa old camping sites and native huts avoided Bedsteads of native manufacture should not be used If the traveller has to sleep on ground he must be well protected by mosquito nets night lights scare away ticks Huts constructed with space of 8–10 in between walls and ground *Floors cemented A deep trench round building filled with* wood ash keeps away ticks Native children frequently act as reservoir of infection **Gammexane** (benzene hexachloride) in water dispersible powder is lethal to these ticks

Prophylactic inoculation—Vaccine cultures of spirochætes from initial attacks and relapses incubated at 37° C for 3 days and kept at room temperature for 16 days 3 injections of 1 0 1 5 *and 2 0 c c at 3-day intervals Possible to produce immunity*

LEPTOSPIROSIS

Infection of blood and viscera with delicate spirochætes (leptospiræ)

Infectious Jaundice—Weil s Disease Spirochætosis Icterohæmorrhagica *A severe fever especially in sewer workers* caused by *Leptospira icterohæmorrhagiæ* with jaundice and enlargement of liver Reservoir rat Canine epidemic gastritis (Stuttgart disease) or canine typhus resembles Weil s disease and has been found increasingly common in man Dog reservoir and may although healthy harbour *L ictero hæmorrhagiæ* and *L canicola* Serum of 27 per cent healthy dogs agglutinates leptospiræ *Canicola* fever found to be widespread in Holland Germany and now recognized in England

GEOGRAPHICAL DISTRIBUTION

World wide especially Japan also England France Germany Common in Holland W Africa Congo N Africa Mediterranean area Egypt Abyssinia Andaman Islands Malaya Dutch E Indies United States Guianas Brazil Peru, Argentine

Epidemiology—Japan September–November Europe summer months Leptospira is common harmless parasite of wild rats mice and dogs found in kidneys and excreted in urine Abundant in polluted water

Most common in farmers miners sewer workers workers in fish factories in Holland in bathers in canals Cane cutters in Queensland

Slime fever —Mild form in summer in Germany Common disease of dogs foxhounds foxes silver foxes leopards and other carnivora which eat rats

ÆTIOLOGY

L icterohæmorrhagiæ in blood urine C S F and sputum Spiral filament with wide flexures the individual spirals in close apposition (20 μ by 0 25 μ—average 6–12 μ) demonstrated by dark ground illumination and Fontana s strain Rapid movements one end straight the other hooked Progress by rotating posterior hook Difficult to demonstrate in human blood but easily found in guinea pigs In sections (especially of liver) by Levaditi s silver nitrate impregnation Cultured on blood agar also chorio-allantoic chick membrane Serological races recognized—status uncertain dog strain *L canicola* (Holland) *L grippo typhosa* (E Europe and Russia) In Queensland *L australis* A and B many strains in Malaya Differentiated by delicate Rieckenberg reaction Rats infected 32 4 per cent Japan 56 per cent. Holland 4 per cent. sewer rats London Dogs 6 per cent. in Sumatra Guinea pigs susceptible puppies rats and monkeys less so Injected intraperitoneally with 3–5 c c of blood animals die with intense icterus on 10th day

PATHOLOGY

Liver enlarged + Gall bladder distended with bile Both icterus and hæmorrhages ascribed to interference with prothrombin production in liver Spleen enlarged with soft diffluent pulp Microscopically cellular degeneration and focal necrosis fatty degeneration not so advanced as in acute yellow atrophy Leptospiræ interstitial and intracellular Enlargement of lymph glands Hæmorrhages into kidneys Petechial hæmorrhages into stomach duodenum and lungs. Secondary anæmia r b c 3 million Great reduction in blood platelets

In inoculated guinea pig hæmorrhages into lungs form butterfly patches

CLINICAL FEATURES

Incubation period 5–6 days Onset acute rigors vomiting headache diarrhœa then fever thirst and aching Characteristic intense injection of conjunctiva (? primary invasion by leptospiræ) Injection of palate agonizing limb pains paræsthesia of gastrocnemii Temperature 103–105 F (39 5–41 C) falling by lysis on 10th or 11th day Secondary terminal rise associated with excretion of leptospiræ from urinary tubules Urine albumin bile casts and occasionally r b c Blood urea + before 10th day Leptospiræ may persist in urine and be scanty in blood Icterus in 50 per cent 48–82 hours from onset jaundice progressing deeper till 9th to 10th days Skin orange-coloured pruritus + morbilliform and erythematous rashes purpura indicates bad prognosis Herpes labialis often Also hæmorrhages into conjunctivæ skin or mucous surfaces In acute forms black hæmorrhagic vomit and hæmaturia. Fæces pale

Bradycardia in later stages blood pressure reduced polymorphonuclear leucocytosis later lymphocytosis Liver enlarged gall bladder distended and tender Splenomegaly exceptional Inguinal and axillary lymphatic glands enlarged

Convalescence in 3rd week Occasional short recrudescences *After fever* allergic phenomenon occasionally

Typhoidal uræmic and meningeal forms In meningeal C S F under increased pressure and contains albumin and leptospiræ leptospiral meningitis fatal cases with paraplegia Meningeal irritation specially common in *L canicola* infections—resembles lymphocytic meningitis

Complications epistaxis melæna hæmoptysis deafness iritis and irido-cyclitis Sequelæ anæmia and debility alopecia Mortality may be 18 per cent

DIAGNOSIS

Blood dark ground illumination for leptospiræ better by triple centrifugation Blood (6 c c) injected into peritoneal cavity of guinea pig—also urine after 12th day Blood filaments often mistaken for leptospira Agglutination test with cultures of leptospiræ 1 500–1 30 000 positive Agglutinins in blood 6–10th day persist for 22 months Macroscopic agglutination also useful Dark ground illumination shows up agglutination Living cultures preferred by Schuffner Complement fixation reaction useful Rieckenberg test (adhesion phenomenon) Urine gives green reaction with 2 drops acetic acid also yields leptospiræ by centrifugation up to 40th day High blood urea (200–300 mgm) Van den Bergh reaction biphasic Leptospira present in urine also by dark ground illumination

Differential diagnosis—From yellow fever (*difficult on clinical grounds*) infective hepatitis syphilis of liver relapsing fever and malaria From Heyd s syndrome—or hepatorenal failure with high blood urea Hess occlusion test is decisive In leptospirosis a petechial rash is alway present above the constriction

TREATMENT

General lines Intravenous injection of glucose and saline Diet liquid Spirits of camphor for pruritus *Penicillin* now considered most successful treatment in 40 000 units with an average of 1 5 mega units by continuous intramuscular drip given early before damage to liver or kidneys has taken place Dramatic improvement in 36 hours

Specific antiserum 20 c c intravenously at intervals of several hours for 4 days for average adult man 60 c c daily Convalescent serum also beneficial

Prophylaxis—Measures against infected rats especially contamination of food Avoidance of abrasion of hands in sewer workers and miners Avoidance of infected water and canals by swimmers. Crawl stroke dangerous

SEVEN DAY FEVER

Autumn Fever—Japan A short fever in summer months resembling infectious jaundice

Geographical Distribution—Especially Japan also India and Dutch E Indies

Ætiology—A leptospira (*L hebdomadis*) distinguished from *L ictero hæmorrhagiæ* by serological reactions In blood in small numbers mainly in urine

Reservoir host in Japan vole—*Microtus montebelloi* Guinea pig susceptible to inoculation

Clinical Features—Conveyed by bite of field voles Fever accompanied by conjunctivitis muscle pains lymphadenitis albuminuria leptospiræ in urine Mild fever of 7 days duration No icterus slight leucocytosis

Diagnosis—By serological tests and by demonstration of leptospiræ in urine Differential diagnosis from infective hepatitis rat bite fever and especially dengue Much confusion with latter dengue rash distinctive

Treatment.—Mild disease Penicillin treatment

RAT-BITE FEVER

Sodoku (Japan) Acute fever caused by *Spirillum minus* by bite of rat sometimes cat or ferret.

Geographical Distribution—Mainly Japan but also in England Germany Italy U S A E Africa Australia

Ætiology—*S minus* small spirillum differs in size from spirochætes (1 5–6 μ) has pointed extremities ending in flagella and 3–4 regular curves Difficult to demonstrate in blood by dark ground illumination but can be found in exudate near bite and in aspirated juice from lymphatic glands Moves rapidly like vibrio

After inoculation of white mice organisms are demonstrated in blood in 7 days Guinea pigs and monkeys also susceptible Probably identical with *S muris* occurring naturally in mice and rats Often forms agglomeration 40–50 μ in diameter Cultivated with difficulty on inspissated horse serum

Some cases are due to *Streptobacillus moniliformis* Haverhill Fever Epidemic and may be milk borne May be conveyed by bite of laboratory rat wild rats or other animals (cats) Incubation period 5 days Wound heals promptly Serum agglutinates *S moniliformis* Curable with penicillin Arsenicals of no value

Pathology—Fatal cases rare Hyperæmia of cerebral cortex and increase of pressure in C S F Spleen enlarged liver hyperæmic lung hæmorrhages In guinea-pigs and rats swelling of lymphatic glands and spleen

ÆTIOLOGY

Sp pertenuis in skin lesions or in serum from papules examined by dark ground illumination stained by Giemsa or Indian ink methods Found in spleen lymphatic glands and bone marrow Rabbits and monkeys susceptible Higher apes reproduce picture of human disease Cultivation difficult has been effected on solidified horse serum Testicular inoculation in rabbits produces lesion similar to syphilis granular or finely nodular peri-orchitis shorter incubation period than syphilis

PATHOLOGY

No visceral changes absence of endarteritis thickening of epidermis degeneration of epithelial cells later hyperkeratosis Papillæ vascular infiltrated with lymphocytes and plasma cells also giant cells

CLINICAL FEATURES

Primary Stage—Incubation period 3–4 weeks granuloma or papule (1–7 cm)— frambœsoma —at site of abrasion or scar on buttock, knee leg arm breast lip or inner canthus of eye—never on scalp breasts of nursing mothers and mouths of babies often on hip or elbow in native women carrying children may be single or multiple lasting 3–4 months Malaise rheumatic pains pyrexia bone pains lymphadenitis W R and Kahn + 3–4 weeks after appearance of primary lesion

Secondary Stage.—Three months after primary Eruption skin harsh dry furfuraceous desquamation then minute papules Yaw or frambœsia of varying size *commences round primary sore* mother and daughter yaw itching + Pleomorphic roseolar or resembling squamous syphilide Lesions symmetrical—auto-inoculation—at angles of mouth axilla arms and inguinal region *never on mucous surfaces* Y papule rounded excrescence encrusted hemispherical or depressed may be circinate Inspissated serum forms crust of yaw spirochætes + Y in sensitive attains maximum in 2 weeks Papular form acuminate papules On subsidence pigmented spots remain sometimes lichenoid eruptions as in syphilis

Tertiary Stage—Y ulceration at site of secondary lesion may coalesce involving leg or ankle Serum W R and Kahn + C S F negative no cellular changes Dactylitis common with onychia and atrophy of nails Foot yaws—crab yaws—very painful subdermal on sole of foot dermis splits in radiating fashion **Gangosa** ulcerous rhino-pharyngitis of palate with destruction of nose associated with bone lesions **Goundou** (especially in children) symmetrical hyperostosis of nasal bones headache sanguino-purulent nasal discharge Swellings may enlarge and obstruct vision May also be diffuse hyperostosis of superior maxilla

Hard palate often affected **Periostitis, osteitis and epiphysitis**—Circumscribed painful periosteal nodes on radius ulna and tibia Diffuse osteitis causes sabre-shaped deformity of long bones especially tibia (boomerang leg) Rarefying osteitis causes spontaneous fracture Periostitis of clavicle noted **Juxta articular nodules**—Fibrotic tumours size of small orange on olecranon lower end of femur etc **Skin lesions**—Depigmented patches on hands feet and ankles are characteristic elephantoid limbs result from scar tissue Synovitis and ganglion frequent. Nerve manifestations as in syphilis, unknown

Immunity—After secondary stage but not permanent

Sequelæ—Aneurysm of aorta neurological manifestations described but very doubtful

DIAGNOSIS

On clinical grounds and demonstration of *Sp pertenuis*

Differential diagnosis—From syphilis always difficult Hutchinson s notched teeth interstitial keratitis and nerve deafness are absent. Y always non venereal From Bejel sometimes difficult this is spread by contact and causes lesions of buccal mucosa and produces circinate lesions of soles of feet hyperkeratosis and depigmentation of dorsum of hands Meningo vascular lesions of brain are not uncommon in children

TREATMENT

Reaction to intravenous or intramuscular salvarsan neosalvarsan etc immediate and striking Also bismuth sodium *tetra* bismuth tartrate (sodium bismuthyltartrate or Sobita) *Combined neo-bismuth treatment* alternating weekly injections as in syphilis *Penicillin* reported favourably especially in primary and secondary stages—large doses 1–2 mega units Less effective in tertiary Procaine penicillin superior more slowly absorbed injections less frequent First day 4 c c (1 2 mega units) then one daily for six days or 2 c c twice weekly for three weeks Penicillin aluminium monostearate (P A M) preparation now recommended Chloromycetin aureomycin and terramycin have also proved satisfactory especially latter when given intramuscularly

Prophylaxis—Isolation and segregation of affected Mass treatment of natives now carried out Nutrition essential

PINTA (Carate)

A spirochætal skin disease characterized by peculiar depigmented patches

Geographical distribution—Tropical America especially along rivers Mexico to Peru and Chile

Ætiology.—*Spirochæta* or *Treponema carateum* (*Sp herrejoni*) closely resembles *Sp pallida* found in skin and lymph glands Stained by Giemsa or Fontana shows flexible cylindrical form with pointed ends 10–12 μ in length with turns 0 6–1 μ wide Attempts to cultivate it have so far failed

Clinical Features.—Eruption symmetrical readily mistaken for syphilis lesions of slow evolution with atrophy W R and Kahn + responds to anti syphilitic treatment Incubation period 7–20 days initial papule Hyperpigmented spots alternate with vitiliginous depigmented patches which may become white or blue (slaty or leaden) usually on face and extremities often over bony prominences knuckles and malleoli Pinta is contagious and affects all ages and both sexes usually in adults 15–25 associated with hyperkeratosis of palms of hands and soles of feet Small patches on mucous membranes Onchogryposis or pigmentation of nails frequent

Diagnosis.—Biopsy of skin and demonstration of spirochæte by scrapings and dark ground illumination

Differential diagnosis.—Especially from syphilis yaws leprosy erythrasma ringworm and pityriasis versicolor

Treatment.—With salvarsan penicillin and bismuth as for syphilis

CHAPTER III

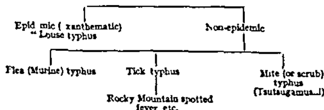
RICKETTSIAL DISEASES

THE TYPHUS GROUP

Comprises numerous closely allied fevers mostly characterized by sthenic character and rash caused by infection with *Rickettsia*

TABLE III

TYPHUS FEVERS



I EPIDEMIC OR EXANTHEMATIC TYPHUS

Acute fever lasting 14 days terminating by crisis pyrexia remittent petechial rash on fifth day

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

World wide common in E Poland and Russia 1917–23 (over 30 million cases 3 million deaths) N W Frontier of India N Africa Belgian Congo Abyssinia Central and S China Manchuria Mexico Gold Coast E Africa Philippine Islands Usually a disease of dirt and bad sanitation in autumn and winter months in conditions of over crowding favourable to louse transmission Brill s disease first described in Jewish immigrants in New York probably mild form of typhus or possibly relapse of original rickettsial infection

ÆTIOLOGY

R prowazeki specific virus conveyed by lice (*P humanus corporis* and *capitis*) filterable from blood plasma and blood platelets during first five days Blood infective for guinea pigs and monkeys Infection conveyed by louse fæces inoculated by scratching Inhalation of dried infected louse fæces is probably capable of causing infection

Transmission —(*see* p 73)

Bionomics of louse —(*see* p 58)

Prophylaxis.—(*see* p 76)

PATHOLOGY

Blood dark, does not clot Toxic damage to liver and kidneys Rash visible post mortem caused by localized necrosis of walls of blood vessels forming typhus nodules (collections of lymphocytes and plasma cells in adventitia) in vessels of skin C N S and myocardium Areas of skin necrosis and gangrene Hæmorrhages in conjunctivæ Spleen enlarged and diffluent Hypostatic congestion of lungs Mesenteric glands enlarged Red marrow hyperplastic and converted into yellow marrow little increase in myeloid elements

CLINICAL FEATURES

Incubation period 4–14 days onset 2 days Headache nausea delirium convulsions T 104 on 3rd day face and eyes congested stuporose drunken expression tongue coated brown epistaxis frequent Urine cloud of albumin increase of urea and chlorides Rash on 5th day on abdomen inner aspect of arms then chest back of trunk face (rarely) palms of hands soles of feet pleomorphic mulberry petechial subcuticular mottling papular or roseolar sometimes may resemble flea or louse bites persists 10 days fades slowly In partially immune population rash may be slight even absent In native races detection is difficult but aided on upper arm by Bier s congestion method by tourniquet Blood moderate leucocytosis 12 000—15 000 mononuclear increase Pseudopositive W R. before crisis Pulmonary complications or bronchitis on appearance of exanthem

Not seen since though similar fever appeared in Weigl s laboratory amongst workers who had been feeding lice (1939) and in E Prussia in second world war

Geographical distribution and epidemiology—Probably identical with Wolhynian fever recognized by Polish physicians before 1914 800 000 cases diagnosed in France 1914–1918 mostly in winter when lice prevalent Group distribution consistent with migratory habits of louse

Ætiology—*Rickettsia quintana* var *wolhynica* conveyed by lice fed on trench fever patients as in I Development in louse takes 5 days

Clinical—Incubation period 2–3 weeks Initial febrile attack followed by relapsing pyrexia Onset sudden pain in back and legs Spleen enlarged by one third No exanthem Tenderness and pain in shins most acute and characteristic *Sequelæ* few and mild usually tachycardia Mortality nil recovery complete

Treatment—By antibiotics as for other rickettsiases

Prophylaxis—DDT as in typhus

IV TSUTSUGAMUSHI MITE TYPHUS

Scrub typhus acute endemic typhus initial eschar at site of bite of mite *Trombicula akamushi*

Geographical distribution and epidemiology—Japan Formosa Korea Malaya Ceylon New Guinea Pescadores Philippines Indo-China Hong Kong Siam Bombay Queensland Men more commonly affected than women especially labourers cane cutters and workers on palm plantations in Malaya particularly after floods and rainy season In Formosa April–November In Japan winter scrub typhus known as Shichito Fever

Ætiology—*Rickettsia tsutsugamushi* (*orientalis*) develops in *leptotrombicula* or *microtrombidium*—larval stage of mite (*Trombicula akamushi*—in Sumatra *T deliensis* and ? *T hirsti*) Infection conveyed in bite through salivary glands Winter scrub typhus in Japan spread by *T scutellaris*

Reservoir host—Wild rats local varieties found infected with *R orientalis* and mite is parasitic on them *R tsutsugamushi* transmitted to guinea pigs and rabbits by intra-ocular inoculation

Transmission—Trombidiidæ—velvet mites—burrow under skin (harvest bugs) Adult trombicula in soil of infected fields 0 9 mm by 0 5 mm pale grey or red with rudimentary eyes four pairs of legs anterior pair stout two pairs of suckers on ventral surface Larva leptotrombicula (*microtrombidium*) 0 4 by 0 25 mm resembles harvest mite in appearance has three pairs of legs (hexapod) covered with minute plumose hairs Larva of *T akamushi* bright vermilion of *T deliensis* pale ochre These mites do not suck blood but on attaching themselves to the skin

inject a proteolytic ferment The skin of the host becomes hardened and a tube (stylostome) is formed in which the mite lies and where it continues to imbibe fluid until it is replete It is the reaction to this digestive fluid which causes the bite to itch

Pathology —Lesion at site of bite coagulation necrosis other lesions resemble those of I except that widespread thrombotic lesions of peripheral blood vessels do not occur Histologically chief change is perivascular infiltration intima secondarily attacked

Clinical —Bite of mite at first not noted larvæ easily seen by magnifying glass with heads and bodies in skin Incubation period 4–10 days malaise frontal and temporal headache then pain and tenderness in lymphatic glands of groin axilla and neck Eschar 2–4 mm surrounded by red areola some lymphangitis T 104–105 F Conjunctivæ injected Bronchitis Splenomegaly Rash 6th–7th day dark red papules on forearms legs trunk—roseolar on face less pronounced on upper arms thighs neck and palate more pronounced than in I Delirium deafness Primary ulcer heals in second week temperature falls by crisis or lysis on 14th day Complications and sequelæ as in I pregnant women usually abort Mortality 20–30 per cent in Japan in Sumatra 15 per cent *N B* —Uninfected mite bites may give rise to irritation at site and mild constitutional phenomena

Diagnosis —As in I Weil Felix reaction OXK (Kingsbury strain) Intradermal test with OXK also employed Initial necrotic ulcer and lymphadenitis characteristic Differentiate from other forms of typhus measles and dengue

Treatment —Site of bite cauterized or excised

Prophylaxis —Mite proof suiting for workers in infected fields mite bites treated with disinfectant (Vleminckx s solution—sulphide of calcium) smearing clothes and exposed parts with dibutyl phthalate proved most successful in Burmese war In Malaya chloromycetin fairly efficient prophylactic 4 gm weekly for a period of 4 to 6 weeks after volunteers had been exposed for 6 days in hyperendemic areas of scrub typhus (Smadel) Aerial photography used for identification and delineation of areas of jungle in which scrub typhus constitutes a hazard Residual insecticides especially aldrin and dieldrin effective in Malaya in controlling the trombiculid vectors of scrub typhus

V TICK TYPHUS—ROCKY MOUNTAIN SPOTTED FEVER

A typhus fever supervening on the bite of ticks *Dermacentor andersoni* and *D variabilis* in U S A

Geographical distribution and epidemiology —Originally thought to be confined to Western States—Idaho Wyoming Utah Now two forms known Eastern and Western latter more severe

Amblyomma small ornate, with eyes widely distributed on lizards and birds has three hosts of same species *Rhipicephalus appendiculatus* dog tick of S Africa resembles *R sanguineus* *Boophilus decoloratus* cattle tick not ornate eyes present *Hæmaphysalis leachi* not ornate eyes absent In adult and larval stages on carnivora especially dogs

Small larval ticks climb on grass and attach themselves to man and animals especially on veld not found on horses or domestic animals Rickettsiæ found in Malpighian tubules of ticks Emulsion produces disease in guinea pigs and *slight* Neill Mooser reation Dog probably reservoir of infection for man

Clinical—Two forms described (1) mild or abortive (2) fully developed In first primary sore adenitis and lymphangitis at site of bite In second in addition fever for ten days with headache, stiff neck conjunctivitis Petechial rash on 5th day

Diagnosis—By Weil Felix reaction (not clear cut) OXK agglutinated in higher titre than OX19 Virus does not immunize against I or II

Treatment.—(*See* p 74)

S American tick typhus, common in Brazil resembles Fièvre boutonneuse Rickettsia transmitted by *Amblyomma cajennense* primary eschar lymphangitis and adenitis mortality 80 per cent Weil Felix not clear cut agglutination with OX19 OX2 OXK Natural reservoirs opossum domestic and wild dog and agouti

Indian form—Sporadic mild form of typhus in N W Frontier of India, from Lucknow and Simla Hills Tick vector unknown at present

VIII Q FEVER (Q=Query)

Noted since 1935 in Queensland Due to *Coxiella (Rickettsia) burneti* now recognized to be identical with *R diaporica* widespread in West U S A and there carried by tick *Dermacentor andersoni* Recently in outbreaks in Greece Turkey Italy Switzerland whole of Central Europe England increasingly common in U S A Congolese Red Fever now shown to be exanthemic form of Q fever

Geographical distribution and epidemiology—*Queensland and U S A* No relationship to season most cases in meat workers and dairy farmers

Ætiology—*C burneti* produces characteristic pathological effects on monkeys mice and guinea pigs In mice enlarged liver and spleen large number of rickettsiæ in intracytoplasmic colonies Smallest of all rickettsiæ and filterable Rickettsiæ cultivated on chick embryo Reservoir host in Queensland bandicoot (*Isoodon obesulus*) specially liable to laboratory infections Transmitted to man by tick *Hæmaphysalis humerosa* in which rickettsiæ occur as natural infection In U S A *Coxiella burneti* var *americana* (*diaporica*) has been isolated from ticks—*Ornithodorus turicata* and *D andersoni* also from spleen of infected merions in Morocco (*M shawi*) Present in pulmonary cases in sputum and can be conveyed to mice and guinea pigs.

Disease is very infectious in Europe and U S A and is there probably conveyed by dust not by droplet Milk from cattle and goats may also convey infection No evidence of any association with ticks in many areas Widespread in sheep goats cattle and buffaloes Isolated from tick *Hyalomma dromedarii* on Sudanese bulls in Egypt also from fæces of sheep and from amniotic and allantoic fluids of these animals in N Carolina and from tick *Ixodes holocyclus* in Queensland In N Africa associated under natural conditions with wild rabbits and tick *Ornithodorus erraticus* found infected

Clinical—Onset acute sudden Pyrexia defervescence 6th–9th day sometimes 4th week No rash or splenomegaly Persistent headache comparative bradycardia In U S A and Europe associated with pneumonitis Mild illness no fatalities

Sera of animals experimentally infected with Australian and American strains agglutinate *C burneti* No cross immunity with V Rickettsia present in human blood during fever and in urine in later stages

Diagnosis—Complement fixation test most reliable Also made by isolation of organism in mice and guinea pigs Radiographs of lungs show evanescent diffuse opacities in central portion over hilum Difficult to distinguish from appearances of atypical pneumonia Pulmonary signs appear clinically in about 50 per cent of cases

Treatment.—(*See* p 74)

IX RICKETTSIALPOX

Described in New York in 1946—pox like rash prominent feature and organism is *R akari* transmitted by mouse mite *Allodermanyssus sanguineus* No positive Weil Felix reaction but complement fixation test is valuable apparently a mild disease no mortality *chloromycetin* is curative

BARTONELLOSIS

Bartonella and rickettsia resemble each other morphologically *Oroya Fever* and *Verruga Peruana* are clinical manifestations of the same disease

(A) OROYA FEVER (CARRION S DISEASE)

Acute specific fever in Andes

Geographical distribution and epidemiology—Latitude 9–16 S elevation 3 000 to 10 000 ft Peru Chile Bolivia Colombia Hot narrow ravines attacks travellers engineers etc

Ætiology—Rod like bodies in r b c and endothelial cells of lymphatic glands *Bartonella bacilliformis* resembles *Theileria parva*—piroplasma—also *Bart canis* of dog Rod-shaped bacillary organism 2 by 0 5 μ with rounded and V shaped forms stained

Cultivation —Glycerin agar, in broth in which butter or coconut oil is dispersed forms *stalactite* growth no spores

Experimental —All laboratory animals susceptible especially guinea pig show œdema round puncture adjacent lymphadenitis hæmorrhagic effusions and death in 24 hours By cutaneous inoculation *die on 3rd or 4th days* Spleen miliary abscesses with plague bacilli + bacilli also in blood

RAT PLAGUE

In epidemics of human plague (esp *bubonic*) rat is important starting point and spread Principal species *Rattus decumanus* (grey Norwegian) and *R rattus* (black rat) mouse bandicoot rat (*Nesokia*) and musk rat play minor part Real reservoir of plague infection is a wild rodent in Central India—*Tatera indica*—which has deep and *extensive burrows* When it comes into contact with the black rat the infection is passed on to it by the fleas which infest it In India *R decumanus* first then *R rattus* attacked then man Seasonal prevalence in rats depends on abundance of fleas Immunity gradually acquired by rat community In plague epidemic all other animals are affected dogs immune

Rats —*R decumanus* (*norvegicus*) (sewer rat) blunt nose short ears *fine hair on rump tail shorter than body Dominant in* W Europe less so in tropics Not closely associated with man burrows under houses in sewers etc

R rattus (ship rat) black in Europe brown in tropics pointed nose large ears cover eyes when folded coarse hairs on rump, tail longer than body climber arboreal, inhabits roofs thatch ships Dominant and domestic in tropics, in close contact with man

Rôle of flea —Plague not communicable by contact Conveyed by rat flea of tropics (*Xenopsylla cheopis* and to lesser extent *X astia*) dog and cat fleas (*Ctenocephalus canis C felis*) Human flea (*Pulex irritans*) is unimportant but occasionally may carry plague direct from man to man without intervention of rat. In temperate climates fleas are most numerous in summer hence bubonic plague is disease of summer and autumn In tropics temperature *above 85° F is unfavourable if dry*

Transmission —In rodent plague bacilli in blood taken up by flea (1) pass through gut viable in fæces (2) regurgitation—more important. Bacilli shelter in proventriculus multiply and form solid plug of bacilli so that the flea cannot swallow When thirsty flea regurgitates bacilli into wound and bites frequently (blocked fleas) due to multiplication of organisms in blood clot in peculiar type of proventriculus

Fleas (*Siphonaptera*) —Wingless blood sucking insects eyes and antennæ much reduced some have combs on head and thorax. Eggs hatch in summer in 3–4 days White hairy larvæ live in dust feed on débris and fæces of adults Fully grown larva spins

cocoon pupates Resting larval stage in which it can remain dormant for months also resting stage in adults *Xenopsylla cheopis* requires higher temperature to develop than other fleas therefore found in heated buildings in England America and Russia Feeds every 10 days In temperate climates hibernates in adult stage thereby may remain plague infected through winter as in rodent flea plague of Siberia Antepygidial bristle on short pedestal Ninth sternite has appearance of a club In female tail of receptaculum seminis is longer than in other species

X astia very similar Male ninth sternite ribbon like In female head of receptaculum seminis much wider than tail Can carry plague but not so effectively as *X cheopis*

Numerous wild rodent fleas capable of transmitting plague such are *Oropsylla silantievi* of the giant marmot In S Africa numerous rodents such as the striped and multimammate mouse have their own species of flea as do the gerbilles In California the ground squirrels harbour *Ceratophyllus acutus* and *Hoplopsyllus anomalus*

Flea prophylaxis —Floors of house washed with solution of naphthalene benzene or emulsion of soap and petroleum diluted with water 1 20 made from soft soap and petroleum 3 pts of soap melted by heat in 15 pts of water 70–100 parts of oil added while hot shaking and stirring DDT spray specially adapted to flea destruction

Cats and dogs in houses should be washed with carbolic soap or strong lather of vermijelli or powdered with naphthalene or dusted with pyrethrum and DDT

For irritation of flea bites apply 1 20 carbolic acid

Cheopis index —Standard adopted by sanitarians=number of fleas per rat Less than 1 indicates rat plague will not easily spread above 1 danger increases over 5 dangerous seasonal variations important general average per annum computed *i e* number of fleas collected divided by number of rats

SELVATIC PLAGUE

Pneumonic plague in Mongolia and Siberia associated with giant marmot (*Arctomys bobac*) and susliks (*Citellus*) which hibernate in deep burrows and harbour *P pestis* killed for skins *P pestis* conveyed by fleas or by aspiration (droplet infection) In Caucasus pouched marmot (*Spermophilus guttatus*) in Transbaikalia *S eversmanni* and *S dauricus* also jerboas and gerbilles In California ground squirrels also tree squirrels marmots and prairie dogs In S African high veld gerbilles ground squirrels and multimammate mouse In lower bush striped mouse and springhaas In Senegal, a shrew (*Crocidura stampflii*) On Gold Coast giant rat Kenya field rat In S America and Argentine cavies such as *Microcavia australis* and *Galea musteloides* as well as other rodents suffer from plague epizootics

spraying for fleas most efficacious measure introduced in liquid form and in dusts For larvæ 5 per cent spray–100 mgm. per sq foot applied to floor and 3 feet up walls

In sylvatic plague California trapping and poisoning (poisoned grain) of infected squirrels In S Africa gassing gerbille burrows

Personal prophylaxis—Isolation of plague cases and contacts Muslin masks with goggles rubber gloves and cotton uniform There is great danger to attendants and contacts in pneumonic plague

Prophylactic inoculation—Haffkine s prophylactic six weeks old culture of *P pestis* at 30° C (86° F) killed by heat + 0 5 per cent carbolic acid 4 c c (64 9 min) Injection causes considerable reaction but gives protection for 20 months

Otten s avirulent living *P pestis* injected Gives minimal reaction Used on large scale in Java similar strain in Madagascar Results favourable

MELIOIDOSIS

A glanders like disease of rodents due to *Pfeifferella whitmori* (also known as *Malleomyces pseudomallei*) accidental in man resembles tularæmia

Geographical distribution and epidemiology—Limited to Burma Malaya Singapore Saigon Guam Ceylon possibly Uganda also found in Berlin Beggars rag pickers and drug addicts in Rangoon Singapore and in hovels in Berlin

Ætiology—*Pfeifferella whitmori* resembles *B mallei* small bacillus same size and shape stained by Leishman on culture (also like *B mallei*) liquifies gelatin Acute orchitis on intraperitoneal injection of guinea pig (Strauss reaction) Laboratory animals easily infected Characteristic discharge from nose and eyes *P whitmori* in urine and fæces

Reservoir hosts—Rat cat dog horse (Intranasal infection)

Pathology—Lesions vary considerably Usually small pulmonary abscesses resembling miliary tuberculosis Nodules in liver resembling portal pyæmia. *P whitmori* in blood urine fæces Cutaneous pustules

Clinical features—

(A) *Acute*—Acute diarrhœa and collapse, resembling cholera Usually high remittent pyrexia Delirium and mania Pulmonary lesions resembling T B

(B) *Chronic*—Lesions confined to skin and subcutaneous tissues Initial sign may be parotitis common in morphia addicts

Diagnosis—By isolation of *P whitmori* from urine fæces and blood also from C S F Serum agglutination + 1 2 500–1 3 000

Differentiation from *B mallei* patients with *P whitmori* give + test to *mallein* while horses with melioidosis give negative Central infiltration with slight tendency to extension characterize melioidosis reaction by subcutaneous injection of *mallein* May be difficult to distinguish from achromogenic forms of *Ps pyocyanea*

Differential diagnosis—From glanders tuberculosis malaria typhoid plague cholera and liver abscess

Treatment—Most die in 10 days Chronic cases are ill for 8 months or longer Chloromycetin now said to be specific

TULARÆMIA

An infectious disease of rodents caused by *Brucella tularensis* transmitted to man by biting flies resembling plague

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Originally discovered in ground squirrels in California and now widely spread in U S A Scandinavia Germany Austria Russia and Japan Mostly in butchers handlers of skins trappers and hunters In U S A and Russia prevalent June to August in Scandinavia July to October

ÆTIOLOGY

Br tularensis small 0 3–0 7 μ Gram negative stains best with Giemsa Cultures on serum glucose-cystine agar best obtained by inoculation of mice and guinea pigs Occurs in enormous masses in spleen Originally classed as *Pasteurella* now allied to *Brucella* group cross agglutination with *Br melitensis* and *abortus* Pathogenic for most laboratory animals and squirrels

Transmission—By gad fly (*Chrysops discalis* see p 227) in Western U S A also by stable fly (*Stomoxys calcitrans*) bed bug squirrel flea rabbit and mouse lice ticks (*Dermacentor andersoni D variabilis* and the rabbit tick) In Sweden by mosquito (*Aëdes cinereus*)

Reservoir hosts—Natural infection in wild rodents In U S.A cotton tail jack and snowshoe rabbits ground squirrel meadow mouse possibly beaver also grouse quail and horned owl In Europe and Asia hare rabbit muskrat water rat field vole In Norway the lemming (lemming fever)

PATHOLOGY

Rarely fatal in man Human pathology unknown Inoculated guinea pigs appearances rather resemble plague Spleen diffusely enlarged necrotic foci with *Br tularensis* stained by Twort s light green and neutral red

CLINICAL FEATURES

Incubation period 1–10 days

1 **Local**—Papule at site of inoculation with secondary lymphangitis May be initial ulcer nodules in lymphatics may resemble sporotrichosis and may suppurate Lymphadenitis of groin and axilla

spraying for fleas most efficacious measure introduced in liquid form and in dusts For larvæ 5 per cent spray–100 mgm per sq foot applied to floor and 3 feet up walls

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CLINICAL FEATURES

Incubation period uncertain may be 6 days but may remain latent for months Initial stage lassitude headache bone pains post ocular pain on lateral movement pain in temporo-mandibular joint sometimes diarrhœa White fur on dorsum of tongue congested pharynx anorexia epigastric tenderness Pulmonary congestion Delirium occasionally usually insomnia Pyrexia remittent temperature rises midday and after (2–4 p m.) Profuse sweats then enlargement of liver and spleen Primary span of fever from 3 weeks to 3 months Intense lumbar pain Fleeting rheumatic pains in joints and fasciæ skin hot and tender no effusion Pressure points especially painful—sacro-iliac joint heels wings of scapulæ supra orbital and intercostal neuralgia Orchitis and epistaxis occasionally Blood changes few in prolonged cases slight secondary anæmia usually slight reduction in leucocytes (6 400) with rise of lymphocytes and reduction of polymorphonuclears

Gradual defervescence with improvement of symptoms succeeded by another febrile bout and so on Undulating fever with ladder like rises to 103 or 104° F (39 5–40° C) Relapses recur for 3–9 months occasionally last a year or longer (average 4 months)

Continued type—High remittent pyrexia without sweats or joint pains rare

Intermittent type—Marked daily excursions not uncommon Sometimes mild rigors may resemble sepsis tuberculosis endocarditis All degrees of severity ambulant mild acute malignant intermittent

Malignant type—Hyperpyrexia and toxæmia Death after one month s duration reported from Sudan

Meningeal type—Rare increased pressure of C S F

Rarer types—Hydrarthrosis of one or more joints without general disturbance occasionally

Surgical—Localized deep abscess on chest wall or elsewhere Chronic osteomyelitis of tibia rare (*Br melitensis* isolated from pus)

Complications and sequelæ—Emaciation, anæmia persistent rheumatic pains especially in sacro-iliac joint Occasionally chronic arthritis sciatica mastitis parotitis ovarian pain dysmenorrhœa amenorrhœa (usually) sometimes menorrhagia Abortion in pregnant women Intermittent hæmorrhages from urethra (inflammation of seminal vesicles) Infection of fœtus recorded Gastric and intestinal hæmorrhage may cause death also hyperpyrexia Secondary complications tuberculosis or pneumonia

DIAGNOSIS

Character of fever and general symptoms

Blood culture—5 c c blood well diluted in nutrient broth (blood clot preferable) incubated for 5 days occasionally positive on 23rd day positive *throughout course of fever* Also obtained by splenic puncture

Urine culture—From second week 5 c c of urine (midstream or catheter) Strict aseptic precautions necessary

Agglutination—Serum heated to 56° C (132 8 F) for half an hour (non specific agglutinins) Zone of pro-agglutination (zone of no reaction in low dilutions) sometimes

Macroscopic test (better) dense emulsion of organism snow flake agglutination rocking slide test preferable (Serum of tularæmia may agglutinate *Br melitensis*) Agglutinations below 1 50 should not be regarded as diagnostic Rising titre of agglutination more important than absolute titre

Intradermal " melitene " reaction—0 2 c c of killed broth culture of *Br melitensis* (500 000 organisms) injected intradermally œdematous hyperæmic zone (4–6 cm) with outrunners visible for several days (+ in 6 hours) Control test with broth and other organisms advisable Weak positive reactions merely indicate sensitization not necessarily infection

N B—Should not be repeated as abscess or skin gangrene may ensue

Animal inoculation—Guinea pig very susceptible

Differential diagnosis—Especially from typhoid by character of fever rapid pulse sweats absence of rash From tuberculosis empyema chronic malaria relapsing fever endocarditis liver abscess

Mortality—2–6 per cent malignant type 10 per cent Continued temperature 104 F (40 C) unfavourable

TREATMENT

General nursing in blanket Liberal diet Hydrotherapy continuous sponging with tepid water Frequent changing of bed clothes

Aureomycin terramycin chloromycetin and other antibiotics cause defervescence of fever and in many cases a cure Alternation of two former advisable in resistant cases A total daily dosage of 3 mgm per kg (about 0 2 gm) 6 hourly is well tolerated Large amounts may have to be given up to a total of 36 gm

Prophylaxis.—In endemic areas milk to be avoided unless sterilized by boiling also sheep s and goat s milk cheese Destroy infected goats *Br melitensis* cultivated from blood or milk *Lacto-reaction* dilute goat s milk 1 200 mix with dense emulsion of *Br melitensis*—agglutination produced

Prophylactic inoculation—3 injections of 500–2 000 million killed organisms

B—ABORTUS TYPE

Milder disease on the whole *Bacillus abortus* (Bang) recognized since 1918 as closely related to *Br melitensis*

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

World wide England Denmark Sweden Germany Holland Switzerland Austria Poland Palestine S Africa Rhodesia Australia

New Zealand U S A (apparently widespread there especially in Michigan) Conveyed in cow s milk sporadic but common in cow men shepherds veterinary surgeons farmers Porcine type in slaughter houses meat packers Chicago and S France

ÆTIOLOGY

Br abortus from blood urine and fæces of patients closely allied to *Br melitensis*

Varieties (a) *Br abortus bovis*—cow from 6 3 per cent of cow s milk
(b) *Br abortus suis*—pig in pig carcases in U S A and England
(c) *Br abortus equi*—? horse

Differentiation —*Br abortus* little larger than *Br melitensis* pleomorphic *Grows best under 10 per cent carbon dioxide tension* Requirements for this diminish on subculture On potato slopes alkaline reaction gives creamy yellow growth (*Br melitensis* and *paramelitensis* brownish or blackish)

Reaction to dyes —*Br abortus bovis* inhibited by thionin
Br abortus suis basic fuchsin methyl violet pyronin.
Br melitensis grows in presence of all four dyes

H_2S production from proteins or amino-acids grown on Staffseth s liver infusion agar at *p*H 6 6 Blackening of lead acetate paper shows presence of free lead

	Carbon dioxide requirement	H_2S *production*	*Inhibition of Growth by Thionin*	*by basic fuchsin*
Br melitensis	—	—	—	—
Br abortus bovis	+	+	Inhibition	—
Br abortus suis	—	++	—	Inhibition

Culture —From milk by cultural method seeded with liver extract peptone agar with 1 10 000 gentian violet in 10 per cent CO_2 atmosphere or by injecting 0 5 c c subcutaneously into guinea pig killed after 3–4 weeks Enlargement of spleen inguinal and lumbar glands contain organisms tubercle like foci Culture from blood or spleen in man comparatively easy more difficult from urine and fæces

Br bovis in cattle Inflammation of uterine mucosa and vaginal discharges Lymphatic spread in udder and teats and in lymphatic glands Also infects genital passages of bull Occurs in epidemic form later chronic and endemic Pregnant cow infected abortion 8–10 days later in chronic type 5–7 months

PATHOLOGY

Same as in *Br melitensis* fever as far as is known Occasionally abscesses of spleen Reticulo-endothelial hyperplasia of lymph glands Meningo encephalitis with greyish white tubercles in *Br suis* infections in U S A

DIAGNOSIS

Cultivation of *Br abortus* from milk and inoculation into guinea pig

Macroscopic agglutination (abortoscope) 1 10 000 dilution with whole blood

Intradermal test (abortin reaction) infiltration and œdema used by veterinarians Diagnosis in man as for melitensis type

Agglutination reaction in low dilutions 1 10–1 80 not diagnostic (? due to absorption of agglutinins in cow s milk)

Blood culture —Precautions as above for *Br melitensis* Blood shows slight leucopenia relative lymphocytosis

CLINICAL FEATURES

Same as in *Br melitensis* type usually milder Short symptomless fevers common May become exceedingly chronic Laboratory infections particularly severe Six types —(1) Mild (2) Classical undulant (3) Abdominal (4) Genital-orchitic (5) Arthritic (6) Catarrhal jaundice type Spleen usually not enlarged Sometimes orchitis and lymphadenitis are sole features Hæmorrhages in severe forms epistaxis hæmoptysis hæmatemesis hæmaturia menorrhagia bleeding of gums purpura jaundice Localized *brucellosis* abscesses in muscles occasionally osteomyelitis Rarefying osteitis of metatarsals rare Meningo-encephalitis reported in U S A Mild cases with temperature 99–100 F (37 5–38 C) headache the only symptom

TREATMENT

Aureomycin and other antibiotics effective as in *Br melitensis* by same method and same dosage Also favourable results reported in *Br suis* infections Some strains of *Br abortus* are sensitive to streptomycin especially when combined with sulphadiazine In S Rhodesia antrypol has been given intravenously in combination with above

Prophylaxis —In dairy herds detection of sick animals and carriers Control of all milk supply necessary but probably impracticable Only solution is universal pasteurization of milk—30 mins at 140–150 F (60–63 C) Problem more difficult in meat packers Prophylactic inoculation not yet inaugurated

BACILLARY DYSENTERIES

Acute epidemic diseases infection of mucosa of large intestine by specific dysentery bacilli Often attended by high mortality

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

World wide not confined to tropics but generally more severe there Certain types found in Europe England and U S A In tropics epidemics in crowded communities prison camps barracks schools bazaars and workers on tea and rubber plantations Nearly always

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present in lunatic asylums Important war disease in 1914–18 virulent epidemic in Gallipoli 1915 also in France During second World War in Poland Russia Near East Palestine Specially virulent in children

Spread —Direct contagion from *fæces* under primitive sanitary conditions and in lunatic asylums from carriers

Flies —Housefly vector of infection feeds on dysenteric fæces and vomits on to food also passes bacilli in dejecta

Water —Medium of infection in Malaya dysentery bacilli can survive in water 3 weeks

Milk —Outbreaks of Flexner and Sonne dysentery in England ascribed to contamination of milk.

Food —Sonne dysentery particularly a food infection in meat and vegetable puddings

Susceptibility of individual —Immunity to infection probably produced by long residence and repeated infection New arrivals in tropics more liable than old residents Bacillary dysenteries are frequently terminal infections in other debilitating diseases such as malaria and tuberculosis

Definite seasonal incidence —In Middle East vernal and autumnal outbreak possibly associated with prevalence of flies In tropics disease of rainy season Also connected with flies waterlogging of soil crowding together of natives in huts increasing chances of infection and risk of pollution of water

ÆTIOLOGY

Shiga s bacillus (Shigella shigæ) characteristic virulent dysentery bacillus rod shaped Gram negative 1–3 μ by 0 4 μ non motile but active Brownian movements Produces acid in milk acid from glucose no indol agglutinated by specific serum and by serum of infected patients Produces exotoxin More frequent in tropics causes most severe forms of disease and greatest number of deaths and complications

Schmitz s bacillus resembles above but produces indol agglutinated by specific serum

Flexner s bacillus (Flexner group) resembles Shiga but less toxic produces acid from mannite and in peptone water indol with exception of Newcastle bacillus which ferments dulcite Has six different strains and antigenic components (Boyd 1938) specific antigen disappears on subculture leaving group antigen Now type specific suspension used for agglutination and other tests Pooled strains

Newcastle bacillus now held responsible for many mild outbreaks of dysentery especially in children in Europe as well as in tropics Differs from other dysentery bacilli in sometimes producing gas in the sugars

Sonne s bacillus is extremely common—especially in children—in epidemic form in temperate zones and also cause of acute diarrhœa

in tropics Ferments lactose saccharose and glucose Agglutinated by specific serum Colonies crenated with lactose media red central point

PATHOLOGY

Inflammation and toxic necrosis of mucosa of large intestine (coagulation necrosis) Usually most intense in rectum and sigmoid but lower third of ileum also affected Gut contracted to narrow rigid tube *mucous membrane olive green brown or black and bile* stained Often irregular in distribution alternating with areas of normal mucosa Lymphoid peritonitis often Toxic damage to liver and other organs Toxæmic nephritis In chronic form ulceration of mucous membrane sinuous submucous tracks in rugose mucosa resembling cobble stones Submucous retention cysts Granulation tissue formation leading to partial or generalized stenosis

Microscopic pathology—Submucosal hæmorrhages round-cell infiltration endothelial proliferation of histiocytes plasma cells apt in sections to be mistaken for *Entamœba histolytica*

CLINICAL FEATURES

Incubation period 1–7 days Onset insidious or sudden all degrees of severity Main symptoms referable to inflammation of large intestine colic tenesmus blood stained mucous fæces Usually pyrexia but in most severe cases often none Tenesmus very distressing Dysuria frequent in severe cases vomiting common Abdomen sunken navicular superficial and deep abdominal tenderness spastic contraction of large intestine especially sigmoid

Stools—Diarrhœa at first then blood and mucus + stools small in amount uncountable in number with pain and straining viscid and gelatinous ones resemble red-currant jelly (to be distinguished from amœbic stool p 46) later exudate becomes more purulent finally in 3rd to 4th week fæcal In most acute and fulminating cases the large proportion of dark blood causes them to resemble meat washings

MILD FORM—Diarrhœa watery stools gradually becoming more mucoid with urgency and griping lasts 1–2 days no pyrexia usually Flexner or Sonne infection

ACUTE FORM—Onset abrupt stools blood stained mucus + griping tenesmus dysuria Pyrexia sometimes rigor Signs of general toxæmia malar flush anorexia furred tongue rapid pulse Navicular abdomen rapid emaciation Attack lasts 2–3 weeks Usually Shiga infection

FULMINATING FORM—Acute and sudden often with rigor Toxæmia from commencement Toxic cyanosis low blood pressure peripheral vascular failure Vomiting initial pyrexia *subsequently subnormal Stools uncountable* much dark blood mousy odour Abdomen at first sunken and acutely tender becomes insensitive Often uncontrollable hiccough Death from toxæmia

CHOLERAIC FORM—Profuse colourless stools resembles cholera

RELAPSING FORM —In certain proportion of subacute cases relapses occur with blood and mucus in stools

CHRONIC FORM —After initial subacute attack chronic diarrhœa occasional blood and mucus emaciation + secondary anæmia In natives associated with other infections (ancylostomiasis and malaria) produces walking skeletons

BACILLARY DYSENTERY IN CHILDREN —Acute and rapidly fatal from toxæmia may be ushered in by convulsions accompanying pyrexia may suggest enterica

Flexner dysentery—*Impossible to differentiate* on the whole from Shiga dysentery generally much milder and complications less severe Newcastle bacillus dysentery resembles foregoing

Schmitz dysentery —Resembles Shiga dysentery

Sonne dysentery —Frequent in England May produce typical Flexner like dysentery pyrexia and toxæmia Fæces greenish or tomato soup Pyrexia and acute onset common continued pyrexia and vomiting resemble other forms of food poisoning Catarrh of respiratory tract bronchitis and rhinitis frequently associated Sonne bacilli numerous in fæces easily isolated Occasionally may cause sudden death in children

Causes predisposing to bacillary dysenteries —Physical exertion unsuitable dietary exposure malaria tuberculosis scurvy enteric

Complications

Dysenteric arthritis (dysenteric rheumatism) frequent in some epidemics (Shiga infections) synovial effusion into joint cavity and tendon sheaths also periarticular with pyrexia and rigor may ensue in acute stage with blood and mucous stools more usually during convalescence after 20th day occasionally all joints affected including interphalangeal and temporo-mandibular resembles acute rheumatoid arthritis May persist 6 weeks or longer rarely causes permanent disability or deformity Differentiation from gonorrhœal arthritis by aspirating *synovial fluid* which is sterile and agglutinates dysentery bacilli in high dilution Arthritis not reported in Sonne infections Peritonitis with serous effusions rare Toxæmic nephritis with albumin and casts in urine and nitrogen retention

Parotitis and intussusception of small intestine common in children.

Perforation of colon rare sometimes chronic peritonitis with effusion

Eye complications —Toxic conjunctivitis in acute stage Iridocyclitis often with arthritis Irregular pupils anterior uveitis photophobia blepharospasm Aqueous humour may agglutinate Shiga bacillus

Sequelæ —Stenosis of bowel and adhesions rarely megacolon Mucous colitis Peripheral neuritis occasionally post-dysenteric tachycardia achlorhydric dyspepsia *Reiter's disease*—a combination of non specific urethritis conjunctivitis and arthritis with fever malaise and raised E S R.—may be independent condition or sequel Arthritis affects larger joints of lower limbs

with effusions and circumscribed areas of tenderness over the periosteum Skin rashes and general lymphadenitis are common There may be recurrences

Carrier state—Dysentery carrier = *convalescent carrier* Incomplete recovery with blood and mucus in fæces Healthy carrier as in typhoid very rare Dysentery bacilli persist in submucous retention cysts Carrier state usually persists 4–6 months maximum about 3 years With improved methods of cultivation (anal swab method) and selective media more carriers recognized than formerly 3–10 per cent in recovered cases In Sonne dysentery more frequent (20 per cent) Rarely granular rectitis persists with blood and mucus passed after defæcation containing bacilli.

DIAGNOSIS

Differentiation from amœbic dysentery most important Apyrexial mild forms without clinical signs may be difficult in absence of laboratory investigations subtertian malaria or other forms may complicate bacillary dysenteries Character of stools helpful microscopic examination of cellular exudate (cytodiagnosis) polymorphonuclear leucocytes with ring nuclei macrophage cells (histiocytes) from proliferated capillary endothelium contain ingested r b c and other débris refractile globular or irregular *apt to be mistaken for E histolytica* *E coli* other amœbæ *Giardia* and the flagellate protozoa may all be found in dysenteric exudates

By culture—Blood and mucus from stool spread on special media (MacConkey Conradi Drigalski desoxycholate agar) recognition of typical round dew-drop like colonies of dysentery bacilli *Specimen must be freshly passed* and free from urine contamination Specimens despatched in tropics should be packed with ice or emulsified with 30 per cent glycerine in 0 6 per cent saline *or* by adding equal volume of $\frac{N}{25}$ NaOH solution rendering them alkaline packed in wide mouthed screw-capped grease proof cardboard tumbler Rectal swabs dipped in saline agar in tumbler assure viability of organisms which by this method remain alive for several days at 15 C Identify colonies by emulsion and macroscopic agglutination with specific serum Subcultures inoculated into solution of sugars—glucose mannite saccharose dulcite Bacilli recovered from intestinal mucosa *post mortem*—not from bile or organs—occasionally from mesenteric glands and blood

Recent experience indicates that best method is combination of fæcal culture with rectal swabs (through proctoscope) especially in Sonne infections Selective media Liefson s desoxycholate citrate medium Superior to MacConkey for Flexner and Sonne

Serological diagnosis—Of little practical value Agglutinins absent in acute cases and often not present till convalescence Most reliable in Shiga cases Shiga positive 1 25 and over diagnostic Flexner 1 100 and over diagnostic More often useful in chronic cases

Dysenteric agglutinins present in cellular exudate in fæces Leucocytosis (16 000–30 000) at commencement of attack, rapidly falling to normal on third or fourth day

Sigmoidoscopy —In acute stages necrosis of mucosa In chronic granular velvety mucosa easily traumatized Bleeding ++ Rigid infiltrated and stenosed lumen Ulceration seldom seen Instrumentation painful In chronic stage differentiation from ulcerative colitis difficult

TABLE V

Differential Diagnosis of Bacillary from Amœbic Dysentery

Bacillary Dysenteries	*Amœbic Dysentery*
Acute disease— lying down dysentery	Chronic— walking dysentery
Incubation period short	Incubation period long
Acute onset with pyrexia	Onset insidious usually apyrexial
Limited disease (2–3 weeks)	Prolonged course
Superficial and deep abdominal tenderness tenesmus +	Localized deep tenderness tenesmus rare
Stools—scanty numerous bright red viscid mucus odourless Red-currant jelly	*Stools*—+ blood and mucus very offensive less numerous larger in amount Anchovy sauce
Reaction alkaline	Reaction acid
Numerous pus and macrophage cells	R b c in rouleaux Macrophage cells scarce or absent few pus cells Charcot Leyden crystals Active *E histolytica*
Blood—preliminary leucocytosis	*Blood*—persistent slight leucocytosis
Sigmoidoscopy—granulation tissue and inflammatory changes in mucosa	*Sigmoidoscopy*—amœbic ulcers in rectum and pigskin pitting

Prognosis —In well nourished Europeans usually good Mortal rate seldom above 5 per cent In ill nourished natives may b 40–50 per cent Prognosis bad if complicated with other disease—*e g* malaria which in bacillary dysentery may be terminal infection

TREATMENT

Nursing in bed essential Preliminary treatment as for shock. Tinct opii or morphia for pain Blood or plasma transfusion beneficial In dehydrated cases intravenous injection of glucose (5 per cent) saline and adrenaline In fulminating dysentery with continuous stools patient should be nursed on mackintosh sheet and packed with tow Bedpan may cause undue distress and straining

Diet —Fluids + meat jellies (Brand s essence) albumin water rice water arrowroot sago milk not recommended Two-hourly small feeds Moro s apple diet recommended in recent war apple pulp up to 2 lbs daily and lemon juice (for vitamin C)

Saline treatment—Saline aperients Sodi sulph ℥ i with water every four hours till stools become fæculent Some prefer *pulv rhei co*

Anti-dysenteric serum—Modern concentrated anti Shiga serum injected intravenously 5–10 c c in toxic Shiga cases Recent experience in favour of combining with sulphaguanidine

Sulphonamides—*Sulphaguanidine* in Shiga and Flexner infections Initial dose 0 1 gm per kilo subsequently 0 05 gm per kilo every 8 hours for 3 days In Middle East 10–20 gm (54–308 gr) daily for 5 days or longer with benefit aggregate 135 gm for each case Mild and acute Shiga infection 20 gm daily for 2 days 10 gm for 3 days Kills dysentery bacilli in lumen of gut Stools become fæculent in 5 days Absorbed by blood in minimal amounts (1 mgm per cent) Therefore toxic phenomena not observed no agranulocytosis occasional purpuric rash Less efficacious in Sonne Cures carrier state If constipated aperients necessary Recommended in chronic stage then may be continued for 12 days or longer Healing of bowel observed by sigmoidoscopy In chronic resistant forms better result obtained by sulpha guanidine retention enemata (5–7 gm 77–107 gr) suspended with mucilage in 7 ozs (296 5 c c) water Other sulphonamides sulphadiazine sulphamezathine and phthalyl sulphathiazole The latter recommended for Sonne Dose 10 gm daily for one week Succinylsulphathiazole 4 gm daily for same period All should be given with plenty of water possibly are less toxic than sulpha guanidine Streptomycin by mouth is poorly absorbed though combined treatment with sulphonamide very effective Local strains of dysentery bacilli should be tested for sensitivity Dose of streptomycin up to 4 years should be 1 gm 4–12 2 gm and for ages above 4 gm in four daily doses for five days 1 gm streptomycin dissolves in 1 dr (3 5 c c) of water Sonne bacillus is more sensitive to streptomycin and this is combined with sulpha guanidine in a preparation—guanimycin

(Bacteriophage treatment much used in India Egypt and elsewhere Results questionable)

Treatment of complications.—Iritis and arthritis on general lines sulphaguanidine beneficial In desperate cases of chronic form appendicostomy ileostomy or cæcostomy used to be performed probably no longer necessary

Prophylaxis.—General sanitation protection of food from flies Elimination of carriers Sulphaguanidine treatment now efficacious especially in Sonne carriers and when combined with saline aperients

CHOLERA

A very severe infectious epidemic disease with a high mortality

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Endemic in Bengal thence epidemics spread over India Has occurred in pandemics all over Europe last in Hamburg in 1892 Has

Bacteriological diagnosis —Microscopic detection of vibrios in fæces
(a) Inoculate into alkaline peptone water incubate for 7 hours
(b) Examine film for vibrios in stained films or by hanging drop
(c) Plate out on alkaline agar (Dieudonné s medium)
(d) Emulsify colonies and agglutinate with specific serum positive over 1 1 000 diagnostic

Bandi s method —Inoculating fæces with alkaline peptone water containing specific serum clumps visible to naked eye form within 3 hours

Short method —Film forming in peptone water emulsified and agglutinated with specific serum on microscopic slide by rotating or rocking (*agglutination forcée*)

Isolation at autopsy —Tie off sections of small intestine aspirate contents and inoculate into alkaline peptone water

Serum agglutination —Not very satisfactory not present in acute stage but in convalescence up to 1 1 000 O agglutinins most important

Differential diagnosis —From food poisoning in latter vomiting precedes diarrhœa Vomit consists of food remains abdominal pain is severe tenesmus frequent and colic invariable fæces are bile stained and offensive but never copious and urine is never suppressed continued pyrexia and no algid stage

TREATMENT

On general lines as for shock In premonitory diarrhœa morphia gr ¼ with atropine gr 1/100

Kaolin —7 oz in 14 oz water sipped frequently stops vomiting

Morphia relieves cramps Hot water bottles foot of bed raised warmed bed pan Suprarenal extract eucortone (I V) 2 c c in 100 c c of 25 per cent glucose followed by saline transfusion

Sulphonamides —Sulphaguanidine in large doses 0 1 gm per kg followed by 0 05 gm every 4 hours Initial dose therefore 5 gm + 2 5 gm at same periods till symptoms subside Sulphathiazole and sulphadiazine also active Condensation product of sulphathiazole and formaldehyde (new compound 6257) strongly recommended Dose 6 gm followed by 4 gm by mouth or rectum Total 28 gm

Intravenous salines —Rogers hypertonic saline based upon blood pressure and specific gravity of blood Normal figure for Europeans 1 058 natives 1 056 Sp G of 1 063 dangerous indicates loss of half blood fluid requiring injection of 3–6 pints subsequent fall indicates further injections (Sp G of blood estimated by bottles of aqueous glycerin from 1 048–1 070 drops of blood remain stationary in centre of glycerin solution)

Composition

Sodi chlor	120 gr (7 6 gm)
Potass chlor	6 gr (0 38 gm)
Calc chlor	4 gr (0 25 gm)
Water	1 pint (591 c c)

at 100 F (38° C)

3–6 pints injected slowly 4 oz per minute Continuous drip trans fusion apparatus preferable Blood plasma and reconstituted plasma now being used Modern opinion considers hypertonic saline unphysiological Now largely replaced by normal saline drip transfusion—three to four pints necessary at one time

Routine treatment with potassium permanganate neutralizes cholera toxin pot permang pills 2 gr coated with salol every quarter of an hour for 2 hours subsequently half hourly till stools become green

Suppression of urine —Maintain B P Pitressin ½–1 c c hypodermically twice daily Caffeine cit gr 5 (0 32 gm) Tinct strophanthus min 5 (0 3 c c) Dry cupping Intravenous hyperalkaline saline sodi bicarb 150 gr (9 72 gm) normal saline 1 pint (591 c c)

Stage of reaction —Digitalin gr 1/100 adrenaline 4–6 mgm Bis salicyl in large doses *Antibiotics* have proved disappointing

Cholera typhoid treatment as for enteric

Bacteriophage (choleraphage) treatment much used in India results doubtful

Anticholera serum of little value

Prophylaxis —*British quarantine system* detention of cholera ships isolation of contacts identification of carriers destruction of fomites and general sanitary precautions In India and Far East wells and water supplies treated with pot permang 60 gr to gallon Recently in India addition of choleraphage to well water Results said to be favourable

Prophylactic inoculation —Haffkine s vaccine 4 000 million dead *V cholerae* ½ c c 10 days later 8 000 million 1 c c Slight reaction Immunity 3–6 months

Immunization per os (Besredka) —Not favoured by British authorities

Personal prophylaxis —General health avoid fatigue chill and excesses unripe or over ripe fruit melons and cucumbers Boil all drinking water (filtration and chlorination insufficient) Treat all cases of diarrhœa seriously

Serological diagnosis—May be complicated in patients previously inoculated with T A B Repeated tests necessary at weekly intervals Agglutinin fluctuates with clinical data progressive rise of titre more important than the absolute Maximum agglutinins between 16 and 24 days Each infection produces specific agglutinin In para A reaction may become positive during convalescence *H* agglutinin heat labile *O* heat stable Vi (virulence) antigen and antibody now recognized H agglutinins mostly produced by passive inoculation O agglutinins (somatic) probably result of active infection with living organisms All Widal tests must now be made with these different emulsions

Auxiliary methods—+ diazo reaction in urine suggestive also Russo's methylene-blue test

Differential diagnosis—From intra abdominal conditions—diverticulitis, appendicitis—associated with polymorphonuclear leucocytosis (enteric group usually shows leucopenia) From *Bact coli* septicæmia (often difficult) Typhus difficult to differentiate in early stages but Weil Felix reaction conclusive Enteric fevers often complicated by malaria bacillary dysentery etc

Typhoid from paratyphoid—No reliable clinical data In typhoid mortality 15 per cent in paratyphoid 2 per cent typhoid more severe and toxic Relapses in para A more frequent longer febrile period than in para B latter often followed by jaundice thrombosis and suppuration Para C diagnosed solely by isolation of organism

Bacteriophage Method of typing—Members of the Salmonella group are susceptible to the action of bacteriophages and they are closely related to the type of O antigen present The Vi antigen of *S typhi* has a special bacteriophage which attacks it so that anti Vi phage grown on typhoid strains of different origin develops a high degree of specificity for this particular strain so that it is possible to obtain a high degree of correlation between the bacteriophage type and the source of the epidemic Vi antigen present in *S typhi* and *S paratyphi* C and it is probable that *S paratyphi* A and B and *S typhi murium* contain Vi antigen specifically susceptible to bacteriophage

TREATMENT

On general lines Milk diet during febrile period Tepid sponging

Chloromycetin (chloramphenicol) in doses of 1 5 gm daily for 4–5 days apparently cures a large percentage of cases The temperature defervesces in 4 days but there is no evidence that it destroys the causative bacilli (*Salmonella*) Recently combination with cortisone advocated—10 7 mg per kg for one day Also combination with minimal doses of aureomycin Ineffective in carrier state

Penicillin in massive doses combined with maximum amount of sulphathiazole given early in the course of the illness and continued throughout has also been advocated

Prophylaxis —Success of anti-enteric inoculation generally acknowledged Typhoid now superseded by triple vaccine T A B 1 000 million typhoid 750 million para A and equal number para B Two doses of 0 5 c c and 1 c c injected subcutaneously at interval of 10 days Reaction slight Recently 3 injections given at weekly intervals Para C also added if necessary T A B C vaccine of Vi strains (Felix) now under trial —

1 000 million	B typhosus	
500	A B C per c cm	
	1st dose	2nd dose
Adult males	0 25	0 5 c c
females	0 2	0 4 c c
Children		
16–18	0 2	0 4 c c
13–15	0 1	0 2 c c
9–12	0 05	0 1 c c
under 8	0 05	0 05 c c

Three weeks interval between injections Re inoculation (booster 1 c c) advisable one year after primary immunization Generally considered that protection lasts 3 years

Hygienic Measures

(1) Detection of carriers and control
(2) Protection of water supplies
(3) Extermination of flies with DDT

ENTERIC LIKE FEVERS

Short paratyphoid like fevers produced by *B alkaligenes fæcalis B ærtrycke* and *B suipestifer Bacterium coli* infections of urinary tract especially common in women in tropics May occasionally assume septicæmic form and organism can be isolated from blood Rigors closely resemble those of malaria

Treatment —Streptomycin probably most effective antibiotic also chloramphenicol in combination with sulphonamides such as sulphadiazine Dosages streptomycin oral in cachets 4 gm daily for 7 days Sulphadiazine—tablets 0 5 gm oral Initial dose 4 gm followed by 1 gm every four hours for the same period

LEPROSY (HANSEN'S DISEASE)

Chronic infective granuloma produced by *Bacillus lepræ*

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Formerly world wide now mostly in tropics and subtropics Lingers in Iceland Norway E Germany Russia S Italy and Greece very prevalent in India and China (0 5–1 per cent) Nigeria Belgian Congo

French Guinea (10 per cent) More virulent when more recently introduced to Sandwich and Pacific Islands Rare in children under 2 44 per cent of older children living with leper parents develop it in their 10-30th year rarely after 40 Primitive natives rarely contract it

Climate little bearing high relative humidity and close contact predispose nodular disease more infective

ÆTIOLOGY

B lepræ=*Mycobacterium lepræ* gelatinous capsule in shape and size resembles T B acid fast decolourizing more rapidly by alcohol Occurs in clusters or zoöglœa masses in lymphatic space arranged like Chinese figures On whole more squat than T B

Demonstrated by biopsy and in smear preparation from exudate in all primary deposits in skin in enormous numbers in skin macules in liver spleen lymphatics lungs endothelium of blood vessels free in blood or enclosed in leucocytes Also commonly in nasal mucus and in nodular leprosy in *apparently normal skin*

Cultivation—Has never been proved Animal inoculation inconclusive Recent work on hamsters slow multiplication in tissues after splenectomy

Differentiation from T B—*B lepræ* group in packets like cigars more solid rarely show coarse granules decolourized by alcohol (with 3 per cent HCl) in 2 hours Gram positive

RAT LEPROSY—Rats subject to disease by acid fast bacillus resembling leprosy in Europe and in tropics House rats affected *R rattus concolor* and *R decumanus* Bacillus cultivated in tissu culture Subinoculation into hamsters Distinct from *B lepr*

PATHOLOGY

Specific lesion of leprosy differs from T B in blood supply, absence of giant cells and of caseation. In section leproma shows round cell with epithelioid and fusiform cells in vicinity of blood vessels majorit of latter contain leprosy bacilli Large swollen cells—*globi*—in whic *B lepræ* have died In maculæ and old lepromata bacilli are scant and the microscopic picture is that of chronic inflammatory change in skin papillæ with characteristic foamy degeneration (foam cells o Virchow) In the neural type fusiform thickening of nerve trunks bacilli in cells and free between axis cylinders eventually nerve become fibrous cords Tuberculoid lesions contain epithelioid an giant cells

In nodular leprosy deposits are found in liver spleen and sometime lungs but lepers are often secondarily infected with T B Teste atrophy *B lepræ* in enlarged hyperplasic lymphatic glands Lardaceous disease of liver spleen kidneys in large proportion of cases of nodular leprosy

CLINICAL FEATURES

Great variety Incubation period difficult to establish shortest probably 3 months usually 2-10 years exceptionally 40

Primary infection and transmission —No visible local lesion but bacillus must enter through breach of surface of skin Possibly nose forms channel of entrance Ulceration of septum and epistaxis frequent Not hereditary children of leprotic parents healthy if removed early from contact Leprosy conveyed by actual contact most Europeans contract disease by sexual relations with native women

Prodromata —Febrile attacks dowsiness dyspepsia diarrhœa or constipation epistaxis nasal discharge pruritus hyperæsthesia pins and needles Areas of sweat suppression (anidrosis) also excessive sweating coming on with slight provocation

Primary exanthem —Evanescent fever and skin eruptions erythematous patches later pigmented may be vitiliginous or bullæ with paræsthesia Loss of hair (depilation) scalp rarely if ever affected Eyebrows and eyelashes often tend to be patchy Primary lesions on face forehead nose cheeks ears extensor surface of limbs Palms and soles seldom attacked Mucous membrance not affected Stage of deposit in skin=nodular in nerve trunk=nerve or anæsthetic leprosy Mixed forms also

Classification now founded on resistance of tissues to leprosy bacillus Low resistance produces definite histological picture of leproma High resistance produces *tuberculoid* Prelepromatous and pre tuberculoid period in which reaction to bacilli is slight known as *indeterminate* Subclassification accordinly of *lepromatous* which is macular infiltrated nodular neural and generalized of *indeterminate* which is macular neural and neuro-muscular of *tuberculoid* macular papular and neural

Lepromatous or Nodular form —This is the severe type
Well marked macular stage Leproma formed in infiltration with round cells in size from pea to plaque many inches in diameter red brown or yellow—usually ham-coloured in white people Centre is anæsthetic to pain and heat devoid of hair greasy looking due to blockage of sebaceous follicles round or oval, but many coalesce forming irregular patches obliterate natural folds of skin on face causing repulsive leonine appearance Nodules on back of hands and extensor surface of arms New crops appear and finally soften in centre which is absorbed leaving smooth circular scar tissue or may ulcerate and discharge yellow pus Septum of nose often destroyed Lepromata on conjunctiva spread to cornea and anterior chamber with destruction of iris and ciliary body Termination usually secondary infection (T B pneumonia bacillary dysentery) Bacillæmia common in advanced cases Hæmagglutination and hæmolytic titres are highest in this type

Tuberculoid type is really the mild type The term tuberculoid is used on account of resemblance to tuberculosis Clinical course depends upon resistance Characteristic clinical feature is tubercle raised above skin surface and dark in colour Tuberculoid skin lesions have sensory changes in tactile pain and heat sensation with suppression of sweat

Nerve leprosy—Prodromal macular stage usually slight or absent When severe annular macular somewhat raised lesions resembling ringworm Bullæ (*pemphigus leprosus*) on hands feet knees etc burst and are converted into anæsthetic patches Implication of nerves neuralgic pains formication hyperæsthesia anæsthesia lymphadenitis Leprotic fever then trophic changes in skin muscle bone Fusiform swelling as thick as little finger on ulnar or other nerves anterior tibial peroneal median radial brachial and commonly great auricular and cervical nerves can be felt and seen lying close under skin at first tender on pressure become entirely anæsthetic Symmetry of anæsthetic areas Temperature of digits affected 2–3 F lower than normal Atrophy of subjacent muscles supplied by thickened nerves with corresponding distortion and loss of power Gradual contraction of fingers causes *main en griffe* Eyelids droop lower everts lachrymation then destruction of lachrymal gland Ulceration and leucoma of cornea blindness Paralysis of lips causing salivation Anæsthetic patches on limbs crack and ulcerate Deformity of nails which become like talons Ulceration of exposed parts rarefying osteitis destruction of toes and fingers absorption of phalanges perforating ulcer of soles of feet Progress very slow Stenosis of larynx produces leper cough and voice

Lepride—Diffuse cutaneous rashes resembling tuberculides probably allergic

Lepra reaction (*Erythema nodosum*) acute with fever in which all lesions become swollen and inflamed usually when infection has become generalized and advanced At same time fresh nodules or macules appear cutaneous and subcutaneous nodules become pustular and discharge pus containing *B lepræ* Reaction may last few days or may be prolonged for weeks Concurrent disease may light up lepra reaction Process may spread to nerve trunks and ramifications Nerves become congested and tender

DIAGNOSIS

Anæsthetic patches especially in centre of macula *Early deposits on forehead* thickening of nasolabial fold Hypertrophy of nipple in men Demonstration of *B lepræ* (acid fast bacilli) in nasal mucus typical morphology and disposition *All acid fast bacilli in nasal mucus not necessarily B lepræ* Biopsy of skin lesions smear preparations Blister of skin by carbon-dioxide snow and demonstration of *B lepræ* in serum also thick-drop blood preparations dehæmoglobinized fixed and stained for *B lepræ*

Blood sedimentation—Rate invariably increased Westergren s method (citrated blood in Wintrobe s tubes at end of hour measure column of plasma left clear by sinking of r b c)

Rubino's reaction—Agglutination sedimentation test with formolized sheep s corpuscles Rapid agglutination and sedimentation in less than 1 hour characteristic of leprosy

In absence of syphilis pseudopositive W R reactions in 63 per cent nodular and 27 per cent. anæsthetic cases but syphilis may coexist

Intradermal Mitsuda (lepromin) reaction with extracts of lepromatous material histologically resembles Mantoux test in T B Material obtained by removing large soft nodules boiling in water and divided into small fragments with scissors dried for few hours and dessicated over pure sulphuric acid 0 4 gm of dried powder is ground up with 10 c c saline and fluid pipetted off and carbolic acid 0 5 c c added Suspension made up in 1 c c ampoules sealed and heated at 120 C for half an hour A series of intra dermal tests with full strength lepromin are made in dilutions of 1 2 1 4 and 1 8 The skin on inner aspect of arm is chosen and the dose is 0 2 c c intradermally The lepromin reaction is of use as a means of testing natural resistance to leprous infection the higher the reading the better the chances of recovery B C G orally converts lepromin negative to positive more frequently than tuberculin negative to positive

Histamine test —Production of histamine in tissues by pinching skin with finger nail Where cutaneous nerves are affected by leprosy the erythematous reaction does not appear in early leprous lesions but shows up as white patches on an erythematous skin

Differential diagnosis —From leucoderma or vitiligo mistake often made no anæsthesia in leucoderma From sensory trophic lesions of syringomyelia spina bifida or hypertrophic polyneuritis with flaccid paralysis of hands and thickened nerve trunks From progressive muscular atrophy lupus tuberculides (inoculation of guinea pig) From other skin diseases acrodynia syphilis erythema nodosum and multiforme ringworms pellagra filarial elephantiasis (*N B* elephantoid condition may complicate leprosy) mycosis fungoides In S America from Espundia (nasopharyngeal leishmaniasis)

Prognosis —Complete recovery exceptional Depends to some extent on nutrition and climate (worse in very cold or hot countries) In nerve leprosy bacilli may die out Disease as in T B burns itself out therefore disease may be arrested Lepers may live 30–40 years Nodular form runs a more acute course Lepers die from nephritis or lardaceous disease stenosis of larynx pneumonia Galloping leprosy death within one year

TREATMENT

Depends upon physical condition nutrition and hygienic surroundings

Sulphones cause striking improvement especially in early tubercu loid cases and even in chronic nodular leprosy as well as in ocular leprosy —D D S or dapsone (diamidodiphenyl sulphone) promin promizole and diasone Careful supervision necessary on account of iron-deficient anæmia Commence with small doses (5 gr) (0 32 gm) in capsules or tablets With hæmoglobin 70 per cent commence with 1 2 3 tablets according to the general condition

of patient (tablets = 100 mg) Initial dose repeated every second day for first week till patient is taking 3 tablets daily for six days a week Iron and liver treatment whenever necessary Maximum average dose is 6 tablets daily for 6 days a week for 3 weeks in every month Prominent nodules and other skin lesions gradually absorbed with gradual diminution in number of bacilli Most striking improvement in eyes especially cornea Cases with negative lepromin reaction become positive

Treatment continued till bacteriological examination negative over period 6 months to 2 years Total length may be 4–5 years Promizole less toxic and quicker in action than promin

Standard induction of treatment is as follows —

100 mg	Dapsone twice weekly for	3 weeks
200 mg		3
300 mg		3
400 mg	maximum	

For those with reactions a maximum of 200 mg for at least three months is advised

Isoniazid (isonicotinic acid hydrazide—INH) 6–8 mg per kg given in combination with dapsone *is considered* beneficial over a period of 2–3 months

Thiacetazone (thiosemicarbazone—TB) no relationship to sulphones Advocated to those intolerant of sulphones Dose 25 mg daily increasing each week by 25 mg till 150 mg Children under 12 half dose Effective also in tuberculosis

Reactions—Lepra reaction occurs mainly in severe lepromatous patients Treatment is by stibophen injections and reduction of dapsone Lepromatous nerve reactions occur mostly when bacteriological smears become negative and give rise to thickened nerves and intractable pain Injections of procaine give relief Tuberculoid nerve reactions are infrequent and are due to caseation Residual hypopigmentation may be mistaken for active leprosy Dermatitis is associated with hepatitis and may lead to cirrhosis Anæmia may occur and is counteracted by ferrous sulphate

Ephedrine—2 gr in gelatine capsules by mouth relieves nerve pains

Carbon dioxide snow—Local application sometimes beneficial

Intranasal therapy—For nasal ulceration ionization of infected mucosa

Co-existing syphilis important—Treat with salvarsan pot iod and penicillin

Surgical measures—

Eyes Division of cornea on pupillary side of lesion prevents extension Tarsorrhaphy for eversion of lids Iridectomy for iritis

Tracheotomy for laryngeal stenosis

Sequestrotomy for necrosis of bone

Amputation for septic ulceration of leg and perf

Prophylaxis—Segregation and isolation of lepers especially in infective state Organisation of leprosaria *Model* Culion Island Leper Colony in Philippines complete with laundry church school etc Much depends on social surroundings Segregation of children of leprous parents Lepers prohibited from selling or handling food laundry work peddling or prostitution Prophylactic inoculation with B C G being tried out

ULCERATING GRANULOMA OF PUDENDA

GRANULOMA VENEREUM (DONOVANOSIS)

Infectious disease transmitted by sexual contact and auto inoculation

Geographical distribution and epidemiology—Widespread in tropics India, Guiana Brazil S America South U S A West Indies New Guinea Pacific Islands N Australia W Coast of Africa S China

Never seen before puberty 14–50 in both sexes especially in women when polyandry is practised

Ætiology—Venereal infection with intracellular organism *Calymmatobacterium granulomatis* (Donovan) (according to modern terminology—*Klebsiella inguinale*) and possibly an intracellular diplococcus (*B mucosus capsulatus*) Non hæmolytic streptococcus frequent secondary invader (Meleney)

Pathology—Histologically allied to rhinoscleroma Nodules at margins of sores masses of inflated round mononuclear cells in Malpighian layer Probably derived from plasma cell containing the organisms demonstrated by Dieterle silver impregnation Vascular growths without hæmorrhages round sebaceous follicles blood vessels lymphatics and sweat glands especially hair follicles

Clinical features—Incubation period short 2–8 days after sexual contact may be prolonged to 12 weeks Primary lesion in genitalia penis labia majora pubes or groin Nodular thickening of skin May occur on face hands or abdomen Excoriates easily exposing granular bleeding surface Extends by peripheral spread and by auto infection of opposing surfaces Predilection for warm moist surfaces such as scrotum labia flexures of thighs Very slow several years to affect large areas Healing by depigmented atrophic scar

In female clitoris vagina labia sterility produced Extends to perineum and rectum profuse acrid smelling discharge No involvement of lymphatic glands Blockage of lymph channels produces elephantiasis of genitalia stricture of urethra and recto-vaginal fistulæ May ulcerate through abdominal wall and invade bladder

Metastatic lesions have been described in Madras in the liver (Rajam) and the organisms have been recovered from this organ Thierfelder has found them in nose ear forehead and mandible Localized deposits have occurred in the middle ear and mastoid process

Treatment—Clean up sore with eusol dressings elastoplast strip Anti-diphtheritic serum 4 000 units injected in vicinity of sores In chronic stage sulphonamide paste Acriflavine ointment, 0 1 per cent in *adeps lanæ*, to this may be added 10 per cent sodi sulph for osmotic effect penicillin

Prophylaxis—Protection of skin against abrasion In mechanized units grease on skin protects against these sores

CHAPTER V

VIRUS DISEASES

Preliminary—Filterable ultramicroscopic particles can be photographed by ultraviolet light and special optical apparatus Larger particles (psittacosis vaccinia) can be stained and measured Many virus diseases of plants birds and animals All viruses associated with living cells and *in vitro* require them for multiplication stimulation of physiology results in active multiplication of cells followed by depression as in cell necrosis of liver in yellow fever Resistance of body to bacterial invasion consequently reduced Specific action may be restricted to cells of one particular organ *e g* rabies for cells of C N S Inclusion bodies in infected cells intracytoplasmic or intranuclear stain intensely with acid dyes (eosin) Cultivation (not possible in absence of living cells) on minced chicken embryo in Tyrode s medium or inoculation of virus on chorio allantoic membrane of chick embryo

Approximate size of virus particles obtained by filtration through gradocol membrane —

Yellow fever	*18 mμ– 27 mμ*
Rift Valley fever	23 mμ– 35 mμ
Psittacosis	220 mμ–330 mμ
Rabies	100 mμ–150 mμ
Vaccinia	125 mμ–150 mμ

mμ = 0 001 μ

Resistance to heat varies extremely resistant to cold survives for months dried Rabies virus resistant to glycerin Inactivated by action of dyes methylene blue Recovery from virus infection associated with long immunity

YELLOW FEVER "AMARYL" (International Nomenclature)

Acute febrile disease endemic or epidemic due to filterable virus with peculiar limited distribution For the most part conveyed by domestic mosquito *Aëdes ægypti*

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

More extensive than formerly supposed Exact range determined by *mouse protection* test Formerly extensive virulent epidemics throughout W Coast Africa Mexico S America West Indies Formerly introduced into Europe Special primitive form—jungle yellow fever—recognized since 1930 Considered in 1925 to have disappeared from S America—not correct Virus exists still in large areas of Brazil Colombia Peru and Central America Recent epidemic in Trinidad accompanied by death of numbers of red howler monkeys (1954) Since 1948 smouldering epidemic of jungle yellow fever has been spreading through Central America Commencing in E Panama it has spread at the rate of 13 miles per month to Nicaragua and Costa Rica to Mexico During the last two years it appears to have fizzled out but in 1956 there has been a recrudescence In Africa the limit extends from W Coast latitude 15 N along S border of Sahara to Blue Nile to Eritræa Massawa and the Red Sea coast thence southward including Somaliland Ethiopia and Kenya Colony to the N shores of L Victoria Thence skirting the E borders of Belgian Congo to a line running through N Rhodesia to Angola Area extends over 4 million sq miles Islands in Gulf of Guinea included Extensive epidemic in Nuba Mts S Sudan (1940) 17 000 cases many deaths in area where not previously noted Danger of transportation in epidemic form by airplane to India or China where disease is unknown

Three epidemiological types —

(1) Urban epidemic transmitted by *Aëdes ægypti*
(2) Rural epidemic transmitted by *A ægypti*
(3) Rural endemic (jungle yellow fever) transmitted by jungle mosquitoes (S America and now W and C Africa)

In (1) and (2) epidemic continues till either all infected mosquitoes are destroyed or high percentage of *susceptible* population become immunized to the virus It therefore follows that the area with a population immune to yellow fever is vastly greater and overlaps the area in which the actual disease yellow fever can be said to exist Hence sudden outbreaks which occur from time to time in W Africa In endemic area disease is present in slight unrecognizable form

Virus of yellow fever readily transmitted but for development in epidemic form requires mean temperature of over 75 F (24 C) Never extends beyond lat 40 N and 35 S Dampness favours spread especially rainy season occasionally occurs in arid areas and up to 4 000 ft

Jungle yellow fever in S America Bolivia Colombia Brazil now W Africa Uganda N Kenya and Congo conveyed by bites of jungle mosquitoes

Reservoir hosts —Recent evidence points to possibility especially in S America that red howler monkeys (*Aloutta seniculus* or *A stentor*) are reservoir outbreaks associated with great mortality in them Virus also found in blood of wild animals in S America opossums edentates some rodents In C and S America monkeys

CLINICAL FEATURES

Great variety In immune or partially immune population may be slight like influenza Onset sudden rigor not usually high pyrexia Attack 3 stages (1) initial fever (2) period of calm (3) reaction

(1) Initial —3–4 days Maximum temperature 2nd day 104° F (40 C) temperature 98–99° F (37–37 5° C) on 3rd 4th and 5th days Rarely maximum temperature not reached till 8th day Supraorbital headache severe photophobia Severe back ache (as in smallpox) Bone pains epigastric pain Face flushed swollen Eyes injected ferrety Skin dry Restlessness Pulse 100–120 bounding *Faget s sign* falling pulse rate with constant T or constant pulse with rising T Tongue white central coating sides clear small pointed palate congested swollen gums swollen bleeding Bowels constipated

(2) Calm —Congestion of face subsides eyes sunken eyelids show ecchymoses Bradycardia 30–40 Skin moist clammy Hæmolytic icterus 3rd day scleræ and skin golden yellow (yellow fever) but not in mild cases where colour is saffron to mahogany brown icterus persists through fever into con valescence Skin has peculiar odour— gun washings fish market often deep blue spots—subcutaneous effusions—or sometimes erythematous papular and other eruptions Erythe matous congestion of scrotum and vulva pathognomonic Diarrhœa often melæna Albumin in urine tendency to anuria on 2nd day in severe cases oliguria with albumin + (2 gm per litre) The more pronounced the graver the prognosis Urine urea 0 15 gm per cent blood urea raised urine acid granular casts Hæmoglobin (spectroscopic) bile pigments 5th day Hæmaturia occasionally Insomnia invariable delirium sometimes torpor in severe cases coma subsultus Sudden rise of temperature presages death Frontal tâche cerebrale visible *Nausea* and *vomiting* more frequent than in other fevers (*a*) bilious (*b*) hæmorrhagic black vomit coffee grounds projectile painless Disintegrated r b c and hæmoglobin in intensely acid yellowish fluid Transudation of blood through gastric mucosa sometimes hæmatemesis Often hæmorrhages from ears nose eyes mouth bladder uterus Everything congested at onset everything bleeds at end Death usual on 5th–6th day seldom before 3rd Sudden fall of temperature after 11th day is serious Period of calm may lead to convalescence Headache back, and bone pain photophobia prostration Recovery usually rapid

(3) Reaction in severe cases —Temperature rises but not so high as initial fever Pronounced icterus black vomit suppression of urine stupor coma often abscesses parotitis or acute hepatitis Spleen not enlarged May terminate in crisis *Sweating* + *Relapses* rare—dangerous No anæmia initial leucocytosis then leucopenia 5th–6th day Polymorphs predominate then mono-nuclears Virus in blood for first 108 hours but has been isolated on 12th day of disease antibody formed in 83 hours Plasma prothrombin shows definite relationship to the severity of the disease Average prothrombin percentage is 66 7

DIAGNOSIS

Easy in epidemic difficult in isolated cases Several deaths with black vomit in limited area in quick succession suggestive Albuminuria important Modern laboratory methods mouse and monkey inoculation positive Suspected blood keeps infectivity for weeks in ice-chest In fatal cases liver changes diagnostic In native races where autopsies not permitted *viscerotome* employed (instrument for obtaining specimens of liver from cadavers for microscopic section)

Differential diagnosis—From subtertian malaria bilious remittent form Discovery of parasite pigmented corpuscles splenomegaly *but* in Europeans in W Africa the two diseases may co exist Sometimes to be differentiated from blackwater on account of hæmoglobinuria From infective jaundice (Weil s disease) not easy often confused From infective hepatitis (no albuminuria) Dengue in early stages closely resembles yellow fever but not so severe Other little known virus diseases in Tunis Nigeria French W Africa Belgian Congo Uganda and Colombia S America may produce fever and jaundice

Mortality and prognosis—Prognosis good if temperature in initial fever does not exceed 105 F Better for women and children than for men for residents than newcomers worse for alcoholics No deaths in cases with fever under 103 F no recoveries with temperature over 106 F (41 C) In some epidemics mortality 50 per cent In natives of endemic zone much less 7–10 per cent Ambulatory cases quite common

TREATMENT

Strict bed Good nursing Injection of immune serum of little value (virus in blood neutralized by immune bodies 4th and 5th day) Purgative at onset (ol ric or calomel 2 gr) Hot bed baths and sponging and mustard plasters to epigastrium relieve vomiting and headache Cold bath and sponging for hyperpyrexia Repeated doses of iron perchloride for black vomit Suggested that vitamin K may be useful Calcium lactate in large repeated doses counteracts excess of guanidine in blood For liver necrosis glucose D repeated doses by mouth or 5 per cent intravenously with injections of insulin 5 units For restlessness luminal phenacetin antipyrine In period of calm alcohol champagne in sips brandy Free fluids for oliguria

Diet.—Liquids only during anorexia afterwards albumin water iced milk or broth If vomiting persistent nutrient enemata Sternberg treatment counteracts hyperacidity much employed sodi bicarb 150 gr (9 7 gm) perchloride of mercury ¼ gr (21 mgm) water 2 pints (1 180 c c) 1½ oz every hour

N.B—Suspected cases of yellow fever in endemic area must be nursed under mosquito net or in mosquito-proof room

Prophylaxis—Destruction of mosquitoes—especially *A ægypti*—and prevention of breeding by every measure Public Health order fines for neglect Introduction of millions (*Gambusia*) and goldfish in reservoirs water butts etc Cisterns screened with

(1) *Invasion* —Malaise very severe rheumatic pains in leg toe fingers knee joint Commences suddenly often rigor deep flushing of face photophobia post ocular pain backache Suffusion of face mucous membrances throat and eyes *Tache cerebrale*=prodromal eruption Prostration in few hours Temperature 103° F (39 3° C)—105 or 106° F rarely Pulse 120 Skin hot and dry Occasional vomiting

(2) *Remission* —Pain disappears temperature normal 3–4 days Tongue clears appetite returns

(3) *Terminal* —Return of fever slight slight or severe bone pains + Rubeolar eruption lasts 3 days followed by furfuraceous desquamation absent in 25 per cent commences on palms and dorsum of hands up arms back of chest and thighs isolated elevated rubeolar spots ⅛–¼ in each surrounded by sound skin— midway between measles and scarlet fever Spots disappear on pressure never petechial Face seldom affected Staining sometimes visible for 3 weeks Bradycardia 40–50 + leucopenia (1 000–2 000 leucocytes) reduction of polymorphs (40 per cent) relative increase of lymphocytes

Convalescence —Rheumatoid pains persist may be permanent periarthritis of knee also in small muscles of hands feet and deep fascia Anorexia mental depression insomnia debility Variability of type in different epidemics some very severe others short fever no rash great variability in epidemic types In some swelling of joints and general adenitis Urticarial and gastro intestinal forms also recognized

Immunity —Not longer than 6 months Repeated attacks common Mortality nil

Diagnosis —Chief danger is confusion with typhus or some other severe fever From yellow fever difficult in early stages From *measles scarlet fever influenza hæmorrhagic smallpox rheumatic* fever or malaria sandfly fever Rash bradycardia and leucopenia are characteristic

Treatment —Symptomatic nursing in bed 10–14 days under mosquito net Liquid diet Diaphoretic mixture *vinum colchici* 15 min (0 93 c c) t d s Cold applications to head Morphia ¼ gr (10 mgm) for pains Urotropine mixture as routine

Prophylaxis —As for yellow fever Measures directed against Aëdes with DDT

COLORADO TICK FEVER AND BULLIS FEVER

The first is an epidemic disease in Colorado associated with *the b te* of the wood tick—*Dermacentor andersoni* The virus is filterable and the clinical features resemble that of dengue *Bullis or Lone Star Fever* is a new form described in soldiers in camp at Camp Bullis near Houston Texas and is conveyed by multiple bites of the tick—*Amblyomma americanum* The clinical features are similar with general adenopathy It is possible that both these diseases may represent a tick borne form of dengue

PHLEBOTOMUS FEVER

Three-day fever Sandfly fever A short fever caused by virus introduced by bite of sandfly (*Phlebotomus*)

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

A disease of sandy waste spaces with a range co-extensive with that of the sandfly where absent disease does not occur *e g* Bermuda In the tropical zone may occur at any time in subtropics in summer and early autumn 75 per cent of newcomers attacked indigenous natives immune Mediterranean area Greece S Italy Middle East Iraq Caucasus Central Asia Chitral N W India (to 4 000 ft) S China Java Brazil and N Argentine

ÆTIOLOGY

Ultramicroscopic filterable virus with same properties as that of dengue allied to but distinct from yellow fever In blood for first and second day of disease can survive outside body 60 hours Monkeys susceptible Undergoes development in body of sandfly No evidence of hereditary transmission through egg of sandfly but larva is infected either by feeding on fæces of imago or by eating dead adults Recently proved in Russia that newly hatched female sand flies are infective It must be emphasized that not all species of phle botomus transmit the disease only (as far as is known) in Europe Middle East and Africa *P papatasii* for there are many species of sandflies in Africa in localities where there is no sandfly fever

Sandflies *Phlebotomus* —In Mediterranean *P papatasii* In most tropical and subtropical countries Minute (1 5–2 5 mm) greyish or brownish slender insects females bite at night males feed on organic matter can pass through meshes of mosquito net Feeble powers of flight range 50 yards Wings folded roof wise Female lays about 40 eggs in rubble cracks in masonry etc In 6–9 days caterpillar like larva appears with two long dorsal bristles Four instars with moults feeds on lizard fæces and carcases of adults pupa orchreous buff Stage lasts 9 days whole cycle 7–8 weeks

PATHOLOGY

No mortality pathological appearances unknown

CLINICAL FEATURES

Incubation period 4–7 days Sudden onset severe rigor Swollen flushed face and injected conjunctiva (dog faced disease —mastiff) Photophobia Fauces congested showing small vesicles Severe frontal headache post-orbital pain stiffness and aching at back of neck influenza like joint and bone pains epigastric pain Band like pain in lower thorax *prominent in recent epidemic in Palestine* reminiscent of epidemic pleurodynia (Bornholm disease) Blood no anæmia leucopenia 3 000 first 4 days then leucocytosis 15–20 000 to 10th day Drowsiness insomnia Bradycardia (40–55)

on 2nd day Temperature 103–104° F (39 5–40° C) for 3 days then crisis, normal on 4th or 5th day usually but fever occasionally lasts up to 8 days At crisis *epistaxis vomiting and sweating diarrhœa.* Serious cases resemble benign lymphocytic meningitis head retraction *Kernig's sign* C S F *pressure increased* lymphocytes 74–300 per c mm albumin + chlorides decreased Debility during convalescence *Sequelæ debility* + acute sinusitis recently observed

DIAGNOSIS

On clinical grounds Slight fever with no rash Very often simulated by mild subtertian malaria also from *dengue paratyphoid typhus* influenza

TREATMENT

No specific *Tinct opii* min 30 (*1 8 c c*) *relieves headache Tinct* iod to sandfly bites Stiffness of neck relieved by lumbar puncture

Prophylaxis—Measures against sandfly DDT is deadly to sandflies *in the adult stages* Burn rubbish demolish ruined walls bury rubble fill cracks with tar fumigate latrines with sulphur Kill adult sandflies by swatting sandfly nets impracticable Camphor on bed and dibutyl phthalate on hands and face repel sandflies

n Army, shorts should not be worn after sundown Wellington boots for legs and ankles Electric fans in barracks and dormitories create upward draught and blow away sandflies—most effective

PSITTACOSIS (ORNITHOSIS)

Originally disease of parrots (especially S American) communicable to man now found in other birds budgerigars pigeons etc

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Outbreaks in England France Germany Switzerland U S A California and probably Brazil S America Australia. *Similar disease* now in Faroe Island and Iceland conveyed by fulmar petrel (*Fulmarus glacialis*) Pigeons ducks gulls finches thrushes and waders (willets) *also found infected Not epizoötic under natural conditions* but only in parrots in captivity in insanitary conditions In budgerigars *especially in cold weather Parrots remain in subacute infectious* state for years Human infection usually directly from parrot but transference of virus from man to man recorded

ÆTIOLOGY

Ultramicroscopic virus (particles 220–235 mμ) *in blood up to 10th* day Other birds—hens canaries finches thrushes—susceptible also guinea-pigs and rabbits mice by intraperitoneal injection intra cerebral injection causes encephalitis Virus bodies stained by Giemsa visible in tissues of diseased parrots and in man

PATHOLOGY

In parrot pericarditis with hæmorrhages Liver studded with white necrotic foci

In man septicæmia with distinctive inflammation of lungs—hæmorrhagic vesicular pneumonia pulmonary thrombosis and muco purulent bronchitis Spleen enlarged diffluent Cerebral purpura

CLINICAL FEATURES

Incubation period 8–10 (occasionally 16) days Severe illness for 2–3 weeks High pyrexia for 7 days Rigors occasionally Epistaxis bone and muscle pains then typhoidal with paroxysmal cough *scattered lung consolidations constipation abdominal discomfort* and semi-coma with muttering delirium Then fall by lysis and improvement in 3 days Mild ambulatory cases reported with sore throat peribuccal œdema and often epistaxis Relative bradycardia Photophobia In some cases rose spots on chest and abdomen 2–4 mm *fading on pressure 7–13th day* No characteristic blood picture Protracted convalescence with liability to femoral thrombosis Mortality 20 per cent

DIAGNOSIS

Not easy many features resemble typhoid also influenza Inoculation of blood and sputum fatal to mice Complement fixation reaction (Bedson)—antigen from spleen of infected mice—is most certain method of diagnosis Pacheco s parrot disease similar but not communicable to mice or man

TREATMENT

Symptomatic similar to typhoid Penicillin chloramphenicol and aureomycetin all effective

Prophylaxis —Prohibition of importation of diseased parrots especially from S America *Difficult in California* where birds (budgerigars and paroquets) may be infected and show no signs of disease

EPIDEMIC HÆMORRHAGIC FEVER (RED FEVER OF KOREA)

Resembles scrub typhus in epidemiology Although known to Russians and Japanese only became familiar to Western Medicine in the Korean War (1952 1953) Cause is not exactly known but is generally thought to be a virus transmitted to man by a mite (*Lælaps jettmari*) and that the reservoir is a field mouse (*Apodemus a rarius*)

Pathology —General vascular collapse Kidneys resemble acute glomerular nephritis albuminuria mononuclear cells and renal tubular cells Kidneys cortex sharply demarcated from medulla Hæmorrhages present

Clinical features —Seasonal incidence Most frequent in May June October and November Fever lasts 7 days recovery in 14 Fatality rate about 13 per cent Fever myalgia albuminuria and petechial rash In severe case hæmoptysis hæmatemesis

hæmaturia and melæna onset abrupt Conjunctival ecchymoses frequent Photophobia and œdema of upper lids intense toxic erythematous blush of face and neck Death due to peripheral vascular collapse

Urine—Albuminuria 28–72 hours from onset persists for one week Specific gravity 1005 albumin 1–4 per cent

Treatment—Symptomatic only Antibiotics and sulphonamides use less Fluids in small amounts on account of increased capillary permeability

IZUMI FEVER

Found only in Japan since 1927 resembling scarlatina Outbreak in Sakishima district south of Tokyo in 1951 Occurs sporadically and in epidemics Characterized by rash temperature chart and gastro intestinal upsets Severe and mild forms recognized Incubation period 5–13 days Onset abrupt with a temperature of 103–104° F (39 5 40° C) Joint pains and lumbar pains vomiting and anorexia Rash in first and second days with itching Slightly elevated papules on flushed skin lasting 3–4 days on trunk face neck and extremities Usually after interval of 2 days rise of temperature with a secondary rash Then periods of sweating with gradual remitting fever for 4–5 weeks Desquamation on 10th day completed in fourth or fifth weeks Hepatomegaly noted in one third Evidence on epidemiological grounds that field mice (*Apodemus speciosus*) may be reservoir of virus Treatment with aureomycin satisfactory

OTHER VIRUS DISEASES WHICH HAVE BEEN DESCRIBED

Durand s virus (D) pathogenic for man and guinea pig Mice easily infected Cultured on chorio allantoic membrane of chick

Bwamba fever in W Uganda Five day fever of sudden onset Pathogenic for mice *West Nile virus* widely distributed in West Nile area Sudan Uganda Kenya Congo Immune bodies in blood of forest monkeys *Cercocebus* and *Colobus*

Meningo encephalomyelitis in Uganda causes paralysis in man and monkeys and is known as Semliki virus and is found in mosquitoes Other viruses isolated from mosquitoes *Aëdes* and *Psorophora* known as Uganda S Bunjamwera Ntaya and Zika

Salisbury fever affects children of 4–9 Acute type of fever (T 104° F) lasting 3–14 days General lymphadenitis with splenomegaly Relapses frequent

POCK DISEASES

SMALLPOX

Severe smallpox now confined to tropics and subtropics Severe outbreaks in India China and Nigeria

Ætiology—Vaccinia now regarded as original virus Variola virus converted into attenuated form by inoculation of monkeys and then intratesticularly into rabbits indistinguishable from vaccinia (cowpox) This transition is not reversible Virus spherical

(0 17 μ) Paschen body Pure suspensions now obtain contain phosphatase and catalase Bodies exceptionally sensit to flocculation by salts Readily vis ble under dark grou illumination Inoculated into skin elementary bodies penetr cytoplasm of epidermal cells increase in number and show aci philic inclusions (Guarnieri bodies) Virus in cells causes hyp trophy and produces papule Later degeneration and liq faction produce vesicle which is then converted into pustule immigration of polymorph cells Fluid forms culture medi for staphylococci and other organisms Crusts or scabs on pust contain active virus High infectivity of smallpox probably to lesions in mouth throat and lungs expressed air conta elementary bodies air breathed by susceptible persons cau infection

Vaccinia and variola cultivated as other viruses in presence living cells in tissue culture of rabbit testes corneal epitheli and in fluid medium of rabbit s serum and Tyrode s solution w minced rabbit kidney Also on chorio-allantoic membrane chick embryo Culture virus inoculated by scarification

Diagnosis —Elementary virus bodies readily demonstrated in ves fluid by dark ground illumination also stained by Gutstei method (1) 1 per cent methyl violet (2) 2 per cent NaHC Dry films in air rinse with normal saline and distilled water d fix in methyl alcohol for half an hour mix equal parts 1 and 2 test tube filter on to slide cover and incubuate at 37 C 30 minutes rinse in distilled water and mount in cedarwood Elementary bodies stained voilet Of no value in differentiat between smallpox and chickenpox

Serological diagnosis —Pocks lightly scraped with scalpel mate suspended in saline clarified by centrifugation then mixed w dilutions of rabbit anti vaccinial serum tubes incubated at 37 Positive reaction finely floccular precipitate Reaction spec for variola and vaccinia Serum of patient in second week disease gives similar reaction No antigenic difference betw true smallpox and parasmallpox

Treatment —Virulence of smallpox largely due to secondary pyoge infection of respiratory tract now treated with sulphapyridi 3-4 gm daily and application of sulphonamide paste to pustu Treatment of smallpox by potent antivaccinia serum under tr Penicillin indicated in pustular stage when infected with penicil sensitive strepto or staphylococci

ALASTRIM AMAAS PARASMALLPOX

Modified smallpox occurring in outbreaks

Geographical distribution and epidemiology —West Indies Bra Central and South America Mediterranean Great Brita Especially in Trinidad Differs from smallpox in rate of sprea smoulders never assuming features of large epidemic Sprea by contact and overcrowding

Ætiology —As for smallpox vaccination protective in high degree

Clinical features—Incubation period 14 days Initial stages resemble influenza and are often mistaken for it Seldom shows the severe headache vomiting and rigors typical of smallpox Eruption 3rd–4th day on buccal mucosa and on skin extends from palate into bronchi Involvement of skin intermediate between chicken pox and smallpox Papules palpated beneath skin Eruption in one crop papules umbilicated crusting at end of first week, and have fallen at end of second or third Distribution centrifugal Protected parts (axillæ groins abdomen) free Face scalp shoulders back arms legs most affected Pocks cluster at site of old scars confluent rashes rare Prodromal rash absent Mortality rate 0 45 per cent

Treatment—Symptomatic only isolation

Prophylaxis—Vaccination most efficient against spread

RABIES (Hydrophobia)

A disease of the C N S in dogs and other animals transmitted to man and animals by inoculation of saliva

GEOGRAPHICAL DISTRIBUTION

All over world in Greenland Iceland and Far North Has disappeared from England less prevalent than formerly in most European countries common in tropics and subtropics in virulent form wherever wild dogs wolves and jackals are common In W Indies and S America paralytic rabies is transmitted by vampire (*Desmodus*) as well as by insectivorous and fruit eating species (*Dasypterus Lasiurus Phyllostoma* and *Artibeus*)

All warm blooded animals susceptible if subjected to bites of foxes jackals wolves dogs also skunks weasels stoats mongoose and rats in S Africa meer cat in North U S A grey squirrel Donkeys refractory dogs camels cattle horses pigs cats sheep goats susceptible

ÆTIOLOGY

Ultramicroscopic filterable virus propagates in nerve endings in neighbourhood of bite Travels up nerve sheaths to C N S primary stimulation then destruction

Street virus—Virus in nervous tissue in naturally transmitted disease Virulence variable when inoculated subdermally into rabbits

Fixed virus—Obtained from street virus by passage through long series of rabbits fixed incubation period constant results One to four Negri bodies in 100 ganglion cells of ammon horn

Negri bodies—Oxyphilic granules in ganglion cells probably same as cytoplasmic inclusions in ammon horn (hippocampus major) used for diagnosis not present in every case only when disease well developed Therefore dogs should not be killed on suspicion but kept till bodies have probably developed

Location of virus—C N S and peripheral nerves infectiousness variable Medulla five times more virulent Salivary glands of infected dogs constantly infectious but not blood fœtus milk urine liver or spleen

C

Cultivation —Difficult obtained in plasma medium in minced chicken embryo and in Tyrode medium

Physical properties —Size 100–150 mμ obtained by centrifugation and concentration heat sensitive when moist in dried form resists 105 C for 2 minutes can resist intense cold and glycerine (50 per cent) for months Sensitive to acids and alkalis

Trinidad disease (Paralyssa)—Paralytic form in cattle and man—transmitted to monkeys Vector saliva of local species of vampire bat (*Desmodus rotundus*)

CLINICAL FEATURES

Incubation period long and variable seldom 10 days may be one year usually 3 months Longer in man than in animals depends on site of bite (proximity to brain) severity of wound and physical condition of patient

Two types (*a*) furiou —excited (*b*) dumb—paralytic

(*a*) **Furious** —Rapid onset insomnia twitchings + pyrexia *Hydrophobia* painful spasms of œsophagus sight and smell of liquid precipitate attack superficial and deep reflexes exaggerated mind clear bouts of mania sexual excitement priapism hoarse voice expectoration noise like bark of dog Convulsive seizures ropy saliva dilatation of pupils respiratory paralysis Average duration 3½ days

(*b*) **Dumb** —Paralytic often unrecognized infection with large amount of virus involvement of spinal cord Pyrexia malaise headache vomiting pain in site of bite numbness ataxia girdle pains consciousness retained creeping Landry type paralysis of limbs trunk bladder face tongue and ocular muscles Death from respiratory paralysis *No hydrophobia* More prolonged than (*a*) lasts 7½ days

Paralytic type most frequent in animals in dogs wavering gait drooping of ears complete paralysis chew sticks and stones swallowing impossible Rabid type marked changes in disposition morose sullen irritable growls barks bites laps water but unable to swallow convulsions death

Immunity —In lower vertebrates rare in man Acquired immunity by inoculation of modified form of rabies virus Virus most virulent for rabbits and after inoculation loses virulence for higher animals Spinal cord of rabbit dried gradually loses infective power Unattenuated *fixed virus* now used for production of immunity no danger of rabic infection

DIAGNOSIS

History Chief difficulty is simulation by hysteria hypersensitiveness to draughts of air suggestive May simulate tetanus and mania Paralytic rabies resembles Landry's paralysis In dogs distemper dog hysteria or brain tumours simulate rabies

Pseudo rabies mad itch —Virus affects ganglia and produces intense itching Non fatal disease has been communicated to man. Psychological rabies recorded in doctors and veterinarians

TREATMENT

No special treatment symptomatic Chloroform inhalations for spasms chloral and bromide *per rectum* and if possible curare subcutaneously Morphia increases mental excitement and suffering Rectal nutrient enemata when swallowing impossible

Prophylactic inoculation of those exposed to infection—Cauterization of wound probably prolongs incubation period and allows time to establish immunity by antirabic inoculation

Preventive inoculation—Production of immunity is long process but incubation period of rabies is normally longer Modification of rabies virus by several passages through rabbits subsequent attenuation of toxicity by desiccation Modern opinion is inclined to the injection of hyperimmune serum to reinforce vaccine treatment The following methods are employed —

(1) Unmodified fixed virus (2) Dilution of fresh fixed virus (3) Fixed virus attenuated by desiccation—original method of Pasteur—dried virus preserved in glycerine In first 4 days two 3-c c injections made daily of dried cord (dried *in vacuo* 14 13 12 11 10 9 8 7 days) Treatment for 21 days (4) Carbolized fixed virus used in India whole brain in solution of 1 per cent phenol in 0 85 per cent saline mixed in mortar at 37° C for 24 hours Suspension stored at 0 C (32° F) Essential inoculation contains 0 5 per cent brain substance Dose 4 c c daily for 14 days Mass vaccination of dogs with chick embryo vaccine in Israel and Malaya is now being undertaken with success The efficacy of both living and killed vaccines has been amply demonstrated *Per se* canine vaccination alone cannot abolish rabies It can have no effect on other animals which really constitute the reservoir of the disease

Indications for treatment—All who have been bitten and who have open wounds scratches etc If animal is alive and *well* for 10 days treatment may be discontinued

Examination of suspected material—Head of suspected dog or other animal wrapped in cloth soaked in bichloride of mercury For inoculation place medulla in glycerine Sections give better result than smears Smears and sections made from hippocampus major are fixed and stained with Unna s polychrome methylene blue for 3 minutes and differentiated in 95 per cent alcohol Negri bodies stain magenta colour

LYMPHOGRANULOMA INGUINALE (L I)

L venereum Lymphopathia venereum Climatic bubo

A venereal disease accompanied by suppuration of the lymphatic glands produced by filterable ultramicroscopic virus

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Very widespread in tropics and subtropics increasingly so in Europe France Germany England Especially in E and W Africa India China Malaya Japan E Mediterranean W Indies and S America and U S A Rediscovered in France as Nicolas Favre disease Infection mostly contracted by Europeans from native women

ÆTIOLOGY

Pus inoculated intracerebrally produces meningo encephalitis in monkeys virus particles contained in leucocytes visible if stained by Giemsa or Castañeda stain also within cells in groups or clusters Developmental cycle of virus particles completed in 48 hours Size 125–175 mμ resemble bodies found in psittacosis Intraglandular injection into guinea pigs produces inguinal bubo intracerebral injection into mice encephalitis also intratesticular and intracerebral inoculation of chipmunks Cultured in tissue culture and in chorio-allantoic membrane of chick From non ulcerative proctitis by insertion of tissue removed by biopsy under skin of guinea pig and reproduction of buboes

Protection test—Equal parts of serum of patient and mouse brain emulsion 1 5 in normal saline kept at 4 C (39 2 F) and 0 5 c c injected intracerebrally does not produce encephalitis in mice

PATHOLOGY

Pin point epithelioid formation and eventually abscesses scattered throughout substance of lymphatic glands Irregularly-disposed histiocytes and giant cells sometimes eosinophiles

CLINICAL FEATURES

Small herpetiform ulcer on prepuce in males heals in few days secondary adenitis Not seen in circumcised In female typical inguinal periadenitis uncommon owing to anatomical arrangement of lymphatic glands Esthiomène and rectal stricture associated with infection—*genito-ano rectal syndrome* Ulceration of vulva with elephantiasis of labia Primary lesion in posterior vaginal wall ano rectal lymphatic glands affected then spreads *via* lymphatics to anterior vaginal wall and posteriorly to rectum Scarring of glands leads to rectal stricture non malignant stricture of rectum invariably due to L I not to syphilis More frequent in Europeans than in natives Eighty per cent give positive Frei Hoffmann intradermal test (*q v*) Extragenital infections on tongue with lymphadenitis of cervical glands in axilla and on foot

Incubation period 3–4 weeks to 2 months Pyrexia of remittent type may precede localizing signs Subacute inflammation of groin glands—unilateral or bilateral—oblique glands first then crural also internal iliac and lumbar Toxæmia from absorption infected glands may suppurate or may subside Periglandular inflammation Fistulæ discharge clear gummy serum If excised heal but may be followed by elephantiasis of leg or scrotum or secondary sepsis Rheumatic painful effusions into knee and other joints noted suppuration may rupture into bladder

TREATMENT

No special treatment symptomatic Chloroform inhalations for spasms chloral and bromide *per rectum* and if possible curare subcutaneously Morphia *increases* mental excitement and suffering Rectal nutrient enemata when swallowing impossible

Prophylactic inoculation of those exposed to infection—Cauterization of wound probably prolongs incubation period and allows time to establish immunity by antirabic inoculation

Preventive inoculation—Production of immunity is long process but incubation period of rabies is normally longer Modification of rabies virus by several passages through rabbits subsequent attenuation of toxicity by desiccation Modern opinion is inclined to the injection of hyperimmune serum to reinforce vaccine treatment *The following methods are employed* —

(1) Unmodified fixed virus (2) Dilution of fresh fixed virus (3) *Fixed* virus attenuated by desiccation—original method of Pasteur—dried virus preserved in glycerine In first 4 days two 3 c c *injections made daily of dried cord (dried in vacuo* 14 13 12 11 10 9 8 7 days) Treatment for 21 days (4) Carbolized fixed virus used in India whole brain in solution of 1 per cent phenol in 0 85 per cent saline mixed in mortar at 37° C for 24 hours Suspension *stored at 0° C (32° F)* Essential inoculation contains 0 5 per cent brain substance Dose 4 c c daily for 14 days Mass vaccination of dogs with chick-embryo vaccine in Israel and Malaya is now being undertaken with success The efficacy of both living and killed vaccines has been amply demonstrated *Per se* canine vaccination alone cannot abolish rabies It can have no effect on other animals which really constitute the reservoir of the disease

Indications for treatment—All who have been bitten and who have open wounds scratches etc If animal is alive and *well* for 10 days treatment may be discontinued

Examination of suspected material—Head of suspected dog or other animal wrapped in cloth soaked in bichloride of mercury For inoculation place medulla in glycerine Sections give better result than smears Smears and sections made from hippocampus major are fixed and stained with Unna s polychrome methylene blue for 3 minutes and differentiated in 95 per cent alcohol *Negri bodies stain magenta colour*

LYMPHOGRANULOMA INGUINALE (L I)

L venereum Lymphopathia venereum Climatic *bubo*

A venereal disease accompanied by suppuration of the lymphatic glands produced by filterable ultramicroscopic virus

*

Rectal stricture in man probably due to introduc rectum at first causes ulcerative proctitis with blo stools Anal stricture more common in women as esthiomene annular and tubular strictures recognized associated with carcinoma most severe are rectal co strictures between bladder and vagina in female and betw prostate and seminal vesicles in male

DIAGNOSIS

From clinical appearances Intradermal Frei Hoffman Pus from aspirated gland mixed with sterile saline (1 5, 60° C (140° F) over waterbath kept at low temperature an from light Potency preserved for three months Also fr gland 0 1 c c antigen introduced intradermally on forear (8–10 mm) control with normal saline and Dmelcos antigen A hard mass of indurated skin persists for few days now also prepared from encephalitic mouse brain inject cerebrally with virus (Findlay) more satisfactory Usual cytosis 27 000

Wassen test fatal encephalitis in mice by inoculation of vi

Biopsy test demonstration of pin point epithelioid formatio giant cells

Complement fixation unsatisfactory

Differential diagnosis —Bubonic plague filarial adenitis soft streptococcal abscess tularæmia lymphadenoma and fe hernia

TREATMENT

1 When discrete surgical excision is rapid and safe Inc contra indicated usually leads to secondary sepsis and formatio intractable sinus

2 Protein shock therapy effective when suppuration has commenc combined with aseptic aspiration T A B 50–300 million organis intravenously 2–3 reactions produced and disappearance of lesio In chronic suppuration application of *unguentum hydrarg*

3 Intravenous tartar emetic 15 injections of 5–10 c c of 1 per cen solution Pentavalent antimony compounds perhaps better bu results uncertain

4 *Sulphonamides* —Sulphapyridine (M & B 693) 1 5 gm (23 gr) daily increase to limit of tolerance average dose in U S A 98 gm (1509 gr) over 34 days Effect on virus (experimental evidence in mice) now generally accepted

5 Chloromycetin and aureomycin are now claimed superior to any other form of treatment in generally accepted dosage (Smadel)

Rectal stricture —May simulate ulcerative colitis In women with leucorrhœa and vaginal ulceration with proctitis sulphonamides —especially sulphapyridine—efficacious Dosage large total 100 gm (1540 gr) in two courses of 15 days Treatment of fibrous rectal stricture more difficult in early stages excision later complete proctectomy and possibly colostomy Diathermic dila tation also employed

CHAPTER VI

FUNGOUS DISEASES

MYCETOMA (MADURA FOOT)

Tropical fungous disease of the foot rarely of hand and internal organs

Geographical distribution and epidemiology—Widespread in India in rural districts Senegal Morocco Algiers Egypt Sudan Somaliland Aden Madagascar Cochin China South U S A S America Occasional cases described in E Mediterranean and S Italy Never in towns always in field workers

Ætiology—Various species of actinomycosis described —

Two main forms of maduromycetoma as distinct from actinomycetoma described Black grained mycetoma—*Madurella mycetomi*—is the common infection with black grains in Tropical Africa India and other Asiatic countries and parts of N and S America

The grains of *M mycetomi* radially spreading septate branching mycelium (1–5 μ diameter) with chlamydospores up to 25 μ in diameter *M grisea* is mainly found in S America In this form the central part is unpigmented surrounded by black cortical zone In the marginal zone the mycelium is embedded in a brown cement Cultural characteristics of these two species permament on Sabouraud s medium The yellow grained fungus is *Nocardia somaliensis* and the red grained is *N pelletieri* (or *Streptomyces somaliensis* and *S pelletieri*)

Pathology—Section of mycetomatous foot express oily surface anatomical elements unrecognizable in pale yellow mass Disappearance of bones network of sinuses and cysts In black variety material is black or dark brown In white it is a white or yellow roe like substance containing mycotic elements

Clinical features—Commences on sole of foot usually at site of trauma as small firm rounded painless swelling (½ in diameter) Ruptures discharges oily purulent bloodstained discharge containing sulphur grains (in black varieties gun powder) Sinuses form general increase of bulk of foot retraction of toes Surface of skin roughened and corrugated Profuse discharge Leg atrophies from disuse May extend to tibia occasionally forearm rarely knee thigh jaw scalp or testicle or lachrymal glands Purulent mucoid fluid exudes containing characteristic grains of the fungus Sinuses develop Regional glands enlarged and infected No fever or other systemic effects

TINEA IMBRICATA TOKELAU RINGWORM —Widespread in natives of S Pacific Burma Formosa S China Central Africa Brazil Requires damp equable climate 80–90 F (27–32 5 C) Fungus *Epidermophyton concentricum* and *E indicum* mycelium cultured by soaking scales in alcohol (5 minutes) in glucose broth and then in Sabouraud s medium Scaly limpet like growth in 3–4 weeks Demonstrated in scales with *liq potassæ* stained by carbol gentian violet Branching mycelium between epidermis and rete malpighii produces concentric scaling

Clinical features —At first confined to one or two spots soon occupies large area and sweeps over whole body with exception of palms soles crutch axillæ and scalp In a year large part of body covered with dry tissue paper scales in concentric parallel lines arrangement characteristic largest scales usually between shoulders Itching + Distinguished from other mycoses by absence of inflammation and by characteristic concentric appearance

Treatment —*Application of liq iodi or chrysophanic acid (20 gr to* ounce) ointment Not found in natives who oil skin with coconut oil

RINGWORM OF FEET

Hongkong foot Mangoe Toe—*Tinea pedis* Originally confined to tropics especially Far East now universal especially in summer months *Epidermophyton interdigitale* resembles *E floccosum* Often associated with mycotic infection of nails and palms of hands resembling Hebra s *eczema marginatum* Isolation of fungus difficult owing to contaminations Now overcome by using potassium tellurite and penicillin to inhibit bacterial growth Causes vesciles between toes and on inner margin or sole of feet macerated skin of interdigital clefts especially the fourth persistent intolerable itching often eczematous secondarily infected Deep cracks may develop Common in swimming and Turkish baths Dermatophytids or sensitivity eruptions may occur in subjects infected locally with fungi This eruption usually subsides on treatment of the primary focus

Diagnosis —Scrapings soaked in *Liq potassæ* recognition of mycelium of fungus

Treatment.—Often difficult Whitfield s ointment (salicylic acid 1 benzoic acid 1 coconut oil 12 paraffinum molle 16 parts) applied for three weeks after feet have been soaked in hot water Cignolin paint tincture of merthiolate and merthiolate cream also much employed

Prophylaxis —*Carbon tetrachloride* applied to lesions said to be rapidly effective Infected persons must take precautions against spread of fungus and should wear loofah slippers in bathroom

As preventive measure application of lotion of liq formaldehyde (40 per cent) ʒ i acid salicyl ʒ i alcohol and water equal parts ʒ viii recommended

TINEA UNGUIUM
Ringworm of nails Common intractable fungous infection by *Trichophyton rubrum* or *T. mentagrophytes*, but several other [illegible] frequently in Europeans in India and China Fungus enters under the free edge of the nail and grows back into the nail bed and invades matrix causing discoloration, ridging and fissuring of nail with friable nails

Microscopic diagnosis —Scrapings made by piece of glass, boiled in *liq potassæ* and soaked for 24 hours fungus elements found especially in dark brown or black spots Liable to confusion with eczema, syphilis, psoriasis and a[illegible] nails due to endocrine deficiencies

Treatment —Scrape nail bed, soften [illegible] by [illegible] and paint with tinct iodi or 2 per cent corrosive sublimate in alcohol, twice daily Dressings kept in position by [illegible] finger stall When advanced only avulsion of nail is effective Nail bed scraped and matrix dressed with acid salicylic or [illegible] ammon ointment [illegible] paint (1 per cent) (Castellani's paint) is well recommended Extirpation of both nails and matrix may be necessary

OTOMYCOSIS [illegible] ear [illegible] ear [illegible] *externa diffusa* usually associated with [illegible] infection of other parts of body Soreness and [illegible] of external auditory meatus pain on contact and on chewing External auditory canal [illegible] with [illegible] discharge In severe cases inject penicillin [illegible] that fungi are main infective agents Most [illegible] *Aspergillus* [illegible]

Treatment —Ear syringed and swabbed with spirit Glycerine and [illegible] tampons inserted Afterwards daily swabbings with spirit and fuchsin paint

TRICHOSPOROSIS

PIEDRA

Peculiar disease of hair of eyebrows, beard and scalp confined to native inhabitants in Brazil, Colombia and Guiana Numerous gritty nodules which look and feel like sand, produces matting and knotting of hair Spore-like bodies and small black nodules on hair shaft due to fungus—*Piedraia hortai* (*Asterineæ*) a family of fungi parasitic on trees Nodule consists of tightly packed stroma of brown hyphæ 4 8 μ in diameter known as *black piedra* demonstrated by soaking in *liq potassæ* easily cultured on glucose agar, liquefy gelatin

Diagnosis —Easy, not to be confused with trichomycosis nodosa or trichorexis nodosa, non-parasitic malformation of the hairs

Treatment —Shaving affected parts

TRICHOMYCOSIS NODOSA —Fungous disease of hair common in Europe, C Africa and Asia, resembles piedra, but produces skin irritation and stains clothes often red Shafts of coarse hairs attacked, usually in axilla Fungus *Trichosporon beigeli*

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OTOMYCOSIS *surfer s ear* *hot weather ear* or *otitis externa diffusa* usually associated with coexisting fungous infection of other parts of body Soreness and redness of external auditory meatus pain on contact and on chewing External auditory canal coated with moist sebaceous discharge In severe cases inject penicillin No evidence that fungi are main infective agents Most common pathogen is *Ps pyocyanea*

Treatment—Ear syringed and swabbed with spirit Glycerine and ichthyol tampons inserted Afterwards daily swabbings with spirit and fuchsin paint

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CLINICAL FEATURES

(1) Primary beriberi diet produced disease
(2) Secondary beriberi now recognized in other forms of peripheral neuritis *e g* alcoholic diphtheritic polyneuritis Korsakoff s syndrome Wernicke s encephalopathy

Predisposing factors—Lowering of body resistance by pregnancy lactation surgical operations convalescence from dysentery malaria or typhoid Breast fed babies suffer from beriberi from deficiency of vitamin B_1 in mother s milk

Incubation period weeks or months Assumes various clinical forms according to extent and position of nerve lesion Onset insidious or sudden usually apyrexial though preliminary pyrexial polyneuritis sometimes noted Mainly two *forms* —

(1) Dry or paraplegic
(2) Wet cardiac or œdematous

1 **Dry**—Paraplegia usually of legs and arms sometimes of inter costal muscles Anæsthesia of front of tibia sides of thighs deep sensibility of tendo Achillis (Abadie s sign) lost Muscular wasting atrophy of gastrocnemii hyperæsthesia of muscles—first gastrocnemii then plantar muscles—fibrillary contractions often myœdema or local zone of contraction on impact Loss of fat Reaction of degeneration (R D) present

Deep reflexes (knee and ankle jerk) absent superficial active Ataxia on walking foot drop often Beriberi of arms causes similar changes loss of muscular power numbness of fingers wrist-drop in extreme cases Paralysis of intercostal muscles serious—death from respiratory complications Paralysis of laryngeal muscles alteration of voice In extreme cases hernia tion of abdomen bulging of perineal muscles on expiration aphonia and explosive cough

Sphincters and bladder normal appetite good digestion normal. Often combined with cardiac involvement

2 **Wet or Cardiac**—Enlargement of heart pulsation of jugulars loud systolic murmurs reduplication of second sound alteration in spacing—tic tac rhythm—acceleration + on exertion dilatation + on exertion especially of R auricle Wide range in pulse pressure low diastolic raised by adrenaline (Aalsmeer s test) used as indication of response to treatment Diastolic pressure = mini mum tone pressure give adrenaline 1 mg observe at 5 minute intervals) Auscultatory murmur persists during complete relaxa tion of pressure Generalized anasarca face puffy lips cyanosed Firmer œdema than that of nephritis not involving scrotum Low tension pulse may be bradycardia Occasionally localized or fugitive œdema associated with neuritis of legs Loss of deep reflexes Amount of urine reduced In subacute or chronic forms gross right sided cardiac hypertrophy pulsation of pulmonary conus and aorta *P* wave accentuated

Cardiac attacks (Shoshin Japanese)—Sudden death from R side cardiac failure + œdema of lungs Also paralysis of diaphragm, acute dilatation of stomach pleural effusion hydropericardium

Postmortem —R heart enlarged conus arteriosus affected Dilatation of veins Intracellular œdema of heart muscle sarcolysis Hydropic degeneration primarily due to excess of lactic acid (defective oxygenation) Primary lesion loss of contractibility due to water retention

Course —Uncertain may suddenly improve then relapse or assume malignant character usually clears up In paralytic form residual pareses or deformity hyperæsthesia and muscular weakness

Mortality —Cardiac form in Malaya high (formerly 80 per cent) paralytic form very low

Atypical forms —Rudimentary forms common partial patchy œdema paralysis of diaphragm ataxia of legs some of mixed type with scurvy and pellagra, *e g* ship beriberi and Rand scurvy Chachaleh of Somaliland is probably mixed beriberi and pellagra

Secondary beriberi —Polyneuritis with alcoholic poisoning gastric carcinoma chronic intestinal obstruction ulcerative colitis (calling for operations on the gastro intestine) cirrhosis of liver and evident alcoholic neuritis Mixed cardiac types common in U S A (curable by vitamin B_1) in polyneuritis of pregnancy with vomiting and in diabetic neuritis Defective assimilation with high metabolic rate responsible for B_1 deficiency Dysfunction of cardio vascular system from unbalanced diet common in U S A and now in Britain Tachycardia bradycardia gallop rhythm vagal reflex irritability dilatation of heart arterial pulsation with pistol sounds Electrocardiograms normal in 7 per cent of cases the main abnormal changes are in the T waves and pro longation of electrical systole Q T

B_1 deficiency plays primary rôle in precipitating disease metabolic rate similar to that of pure carbohydrate diet Cardiovascular syndrome disappears before polyneuritis

Infantile beriberi —Distinct form in Egypt Philippines S China Pacific Islands—scourge of Philippines Differs in essentials from other forms Never in Europeans rarely in half-castes in breast fed infants born of mothers affected with beriberi or on deficient diet causing absence of B_1 in milk When children removed from breast or artificially fed cure results Acute type resembles cardiac beriberi lasts ½–3 months child dies in convulsions Acute heart failure cyanosis head retraction and aphonia are marked features ascribed to paralysis of left recurrent laryngeal nerve from pressure of left auricle

Chronic form —Progressive weakness and wasting with periodic vomiting No true paralysis but loss of knee jerks Pyrexia vomiting and dysphagia presage death

Infantile beriberi appeared in Pacific phosphate islands when restric tion on toddy (fermented coco nut sap) deprived natives of source of B_1 Balance restored by yeast preparations and cod liver oil

Wernicke's encephalopathy—Ataxia clouding of consciousness and ophthalmoplegia = superior hæmorrhagic polioencephalitis originally associated with chronic alcoholism Does not resemble infective encephalitis Post mortem hæmorrhages found in mamillary bodies of brain First symptoms persistent anorexia followed by vomiting and nystagmus then paralysis of external rectus loss of visual acuity papillœdema ptosis and retinal hæmorrhages Rapid response to aneurin injections

Nutritional retrobulbar neuritis—Loss of visual acuity with disorders of perception Usually pain and blind spot in retina Paracentral scotoma degenerative pigmentary changes round macula—occasionally optic atrophy Associated in majority of cases with cardiac beriberi though response to aneurin therapy disappointing

Burning Feet—Chronic condition as ociated with dietetic deficiencies noted with beriberi as well as with pellagra common in detention camps in last war in Far East Deep aching in soles of feet spreading like toothache to instep and toes Pins and needles worse at night usually sleep impossible Ascending skin analgesia exaggeration then loss of deep reflexes Many develop retrobulbar neuritis and most have associated ariboflavinosis Although nicotinic acid gives temporary relief only real improvement is seen with large doses of aneurin

DIAGNOSIS

In epidemic not difficult in sporadic cases by œdema of shins palpitations cardiac irregularity Jongck (squatting) test—inability to rise from squatting position—hyperæsthesia of calf muscles impairment or absence of knee jerk and blood pressure tests —

(1) Increase of diastolic sound after injection of adrenaline
(2) Estimation of diuresis in fasting state with 1 litre of water

Both restored to normal by injection of B_1

Therapeutic test—Administration of adequate B_1 for 10 days Pyruvic acid determination in acute beriberi 2 mg per cent in chronic beriberi 1 5 mg per cent

Differential diagnosis—From other forms of polyneuritis—alcoholic diphtheritic arsenical—triorthocresyl phosphate poisoning (ginger or jake paralysis) flaccid motor paresis tabes dorsalis pellagra nutritional œdema nephritis myocardiac disease epidemic dropsy (*q v*) diabetic neuritis Korsakoff s syndrome Landry s paralysis Chronic lead poisoning shows the blue line wasting of arms with exception of supinator longus also basophilic stippling of r b c Beriberi distinguished from lathyrism by presence of knee jerk Cardiac beriberi occasionally simulated by fluke infection (*Heterophyes* *see* p 190)

Prognosis—Danger signs dilatation of R heart pulsating jugular dilatation of stomach cyanosis dyspnœa paralysis of intercostal muscles scanty urine vomiting

TREATMENT

Dry beriberi.—Diet Elimination of white rice and substitution of peas beans oatmeal yeast (*marmite*) proteins eggs milk fat Strict bed in severe paralytic and cardiac cases Aneurin (B_1) specific best injected subcutaneously Soluble preparations of B_1 given by mouth are destroyed in stomach to great extent *Betaxan* or *Benerva* for injection (25–30 mgm daily) contains 2 mgm aneurin per c c Total amount of aneurin arbitrary depending on extent of paralysis (excretion of aneurin in urine now estimated with accuracy by thiochrome method rapid excretion for 3 hours *after subcutaneous or intramuscular injection*)

For atrophy of muscles faradism and massage after hyperæsthesia has abated Hot air baths also Prevention of deformity from muscle contraction and foot-drop by Phelps s talipes splint with elastic accumulator

Cardiac beriberi.—Nurse as cardiac case For orthopnœa restriction of fluids saline aperient For cardiac distress 3–5 min of 1 per cent nitroglycerin—Ouabaine gr 1/240 (0 27 mgm) intravenously Inhalations of amyl nitrite bleeding abstraction of 8–10 oz (236–295 c c) of venous blood oxygen inhalations

Specific treatment.—Aneurin maximum dosage 3 000 I U (international units p 147) In acute cases 1 000 I U intravenously into jugular vein patient is restless after injection effect is noted in one hour rise of systolic and diastolic B P and corresponding increase of urinary flow Repeat for return of symptoms

Striking results of treatment.—Mortality rate formerly 80 per cent now less than 8 per cent Recovery usually in 14 days Diet must be radically altered no white rice permitted or relapse will recur

Infantile beriberi.—Infants removed from mother to wet nurse Extract of rice polishings 5 c c daily as long as aphonia persists Aneurin (if procurable) 1 mg daily Although symptoms alarming recovery takes place in 3 days

Prophylaxis.—Government control of rice Too much milled rice not permitted Educational methods advisable Accessory foods encouraged Diets containing large proportion of starch and sugar supplemented by foods containing B_1 Bread made from whole wheat flour contains B_1 When maize constitutes staple dietary meal should contain germ Prophylactic *marmite* in cubes (¼ oz 7 7 gm) twice weekly Tinned meat is deficient in B_1 and addition of other foodstuffs necessary

Body possesses no ample reserve of B_1 constant supply must be maintained

SCURVY

Deficiency due to absence of vitamin C (ascorbic acid) characterized by swelling of gums hæmorrhages into skin and mucous membranes Identical with infantile scurvy In tropics occurs in epidemic form amongst labourers and workers on unsuitable dietary especially natives accustomed to liberal fruit and vegetable diet

ÆTIOLOGY

Typical food deficiency Ascorbic acid (now prepared synthetically) hexuronic acid $C_6H_8O_6$ I U = 0 05 mgm Destroyed by prolonge heat and drying present in all vegetables and fruit especially orang and lemon absent from tinned fruits preserved vegetables (peas an beans) Little in milk and meat Cannot be synthesized by mos mammals Reappears during germination of yeast and is synthesize by plants Soluble in water and alcohol more stable in acid than in alkaline media Necessary for elaboration of collagen in tissues for dentine for osteoid matrix chondromucin and cell respiration

Requirements for man = 400 units daily
, child = 800–1 000 units daily

Normal persons have store of vitamin C Normal output 33 mg daily In large doses causes increase of urinary secretion in scorbutics excretion diminished

CLINICAL FEATURES

Period of development 4–8 months Onset insidious loss of weight emaciation weakness pallor stiffness in leg muscles swelling of gums fungating masses project beyond teeth which loosen and fall out Swollen tongue enlarged salivary and lymphatic glands Skin dry and rough Albuminuria and constipation usual sometimes diarrhœa

Hæmorrhages—Subcuticular bruising purpuric rash petechiæ round hair follicles especially on thigh intra articular effusions into knee subperiosteal nodules œdema of ankles Hæmoptysis or hæmatemesis Cardiac distress irregular pulse hæmic systolic murmurs Headache early delirium later Necrosis of jaw in advanced disease

Complications—Gangrene of lungs from septic inhalation Night blindness frequently ascribed to vitamin C deficiency in tropics May co-exist with beriberi sprue pellagra and other diseases
In children scurvy rosary at junction of costal cartilages separation of epiphyses of long bones

Varieties— Rand scurvy no spongy gums or neuritic signs of beriberi primary hypertrophy secondary dilatation of heart Reflexes exaggerated Predisposition to bacterial infections especially pneumonia

DIAGNOSIS

On clinical grounds easy Constriction of arm by band of sphygmomanometer compresses arm to 90 mm on fading of cyanosis petechial spots become visible indicating capillary permeability

Intradermal test—Dichlorophenol indophenol 1/100 c c injected time for decolourization of tissues is measure for vitamin content 5 mins = tissue saturation 10 mins or longer = vitamin C deficiency

Estimation of vitamin C saturation in normal person large dose causes rapid excretion in urine in scurvy retained in body Give 600 mgm ascorbic acid urine in 3–6 hours should contain 5 mgm per cent (titrate against dichlorophenol indophenol)

Differential diagnosis—From acute myeloid lymphoid leukæmia or hæmorrhagic diathesis

TREATMENT

Chiefly dietetic Fruit vegetables lemon juice fresh meat germinating peas Ascorbic acid by mouth or intravenously 40–100 mg (0 6–1 54 gr) daily Hydrogen peroxide mouth wash for gums

INFANTILE BILIARY CIRRHOSIS

Geographical distribution—Frequent in India General features resemble Lænnec s cirrhosis nutritional basis indisputable Also in Dutch E Indies sparingly in Mexico and China

Ætiology—Prevalent in Hindus (not Moslems or Europeans) especially vegetarians and overfed and pampered children aged 6–24 months usually commences during dentition fatal in from 3–8 months rarely may commence within few days of birth and be fatal in 3 weeks Both sexes equally susceptible Family disease In Bengal Bombay and United Provinces commoner in rural districts than in towns Possible connection with cows milk breast fed children escape Association with bacillary dysentery suggested Urine may contain *Bact coli* and *B alkaligenes* *B coli* also isolated from liver Now suggested that fatty liver disease in childhood (malignant malnutrition) may later lead to biliary cirrhosis

Pathology—Intercellular lobular biliary cirrhosis (Lænnec) Formation of new bile-ducts subacute toxic cirrhosis regeneration adenomata of hepatic cells Liver small hard and bile stained Compensatory splenomegaly usual Ascites +

Clinical features—Onset insidious Ascites œdema of hands feet and eyelids Cholæmia icterus pyrexia usually thirst clay-coloured stools urine bile + and occasionally *B coli* Deep bronzing as in Addison s disease Terminal gastro-intestinal hæmorrhage Death from cholæmia

Blood—Microcytic anæmia leucocytes 8–14 000–50 000 in terminal stages mainly lymphocytes Arneth count shift to left W R negative

Treatment—Substitution of modern infant foods for cows milk has *prevented further cases in cirrhotic families Recovery follows* change of food in 6–10 weeks

Prophylaxis—Proper feeding of expectant mothers 2–3 oz fresh fruit daily (Vegetables deficient in India) Iodized salt added to food

PELLAGRA (ALPINE SCURVY)

Endemic disease of slow evolution diet deficiency *Comple* syndrome nervous alimentary and cutaneous with seasonal in cidence Confined to rural population As in beriberi has two stages (1) primary (2) secondary

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Almost universal *Europe* Spain Portugal S France Italy Austria Hungary Balkan States Poland Russia Also a few from German and Britain *Africa* W Africa Egypt Sudan Red Sea Rhodesia Nyasaland Zululand Union of S Africa Tanganyika Kenya Gol Coast *Asia* Asia Minor *India* (*sparingly*) *Malaya Philippines* Japan China Korea Manchuria *America* Canada South U S A Mexico Central and S America W Indies (esp Jamaica Barbados) *Australasia* a few cases in S Australia and New Caledonia

Fluctuation from year to year Long periods of quiescence Not infectious or contagious In epidemic form in spring and autumn months Egypt April–May October–November Nyasaland August–October January–March Barbados May–October

Sex and occupation —Both sexes liable in U S A more in women (17–40 from debilitating effects of menstruation parturition etc) Common in children in South U S A Field labourers especially liable inhabitants of towns escape even in heart of endemic areas

Pellagra in Britain —Attention was drawn to pellagra in England in 1912 then it was discovered in London hospitals later in lunatic asylums and other institutions especially Lancashire Mental Hospital From 1922 onwards numerous deaths from pellagra recorded in asylum inmates Secondary pellagra now commonly noted associated with chronic intestinal disease

Infantile pellagra —Especially in Central W and E Africa sometimes considered a separate disease

Predisposing causes —In time of stress and war great increase in pellagra as in Turkish armies in 1918 noted also in national disasters as after great Mississippi floods *in 1927* Pellagra disappears under improved hygienic and dietetic conditions *e g* in Italy

ÆTIOLOGY

Formerly ascribed to consumption of maize first in Italy later in South U S A Certain proof that disease is still most common in countries where maize is staple article *Influence of sunlight on skin* manifestations noted by Italian observers who reproduced rash on limited areas of skin exposed to sun In 1912 Funk first suggested analogy between pellagra and scurvy as food deficiency Later disease reproduced in America on protein *deficient diet* Biological protein value theory tested out in Turkish prisoners of war in Egypt in 1919

Black tongue disease of dogs (canine typhus) found by Goldberger to be analogous to human pellagra curable by yeast and liver (1922) P P (pellagra preventive) factor stipulated proved identical with vitamin B_2—nicotinic acid and nicotamide

Nicotinic acid —Carboxylic acid of pyridine (by oxidation of nicotine) essential substance in meat infusions necessary for growth of bacteria Nicotinic acid and nicotamide cure black tongue in dogs nutritional disease of pigs and pellagra in man Functions in body unknown but nicotamide part of molecule and co-zymase are essential for carbohydrate metabolism Liver kidneys milk eggs and cheese are richest sources of nicotinic acid

Riboflavin (lactoflavin) —Also concerned in pellagra syndrome a yellow fluorescent pigment in liver eggs and milk imparts greenish colour of whey Isolated in pure state and synthesized Chief supply derived from meat and milk Characteristic sign of riboflavin deficiency in animals failure of growth Concerned with oxidation in body tissues not synthesized by the organism essential for cellular respiration Deficiency in man (aribo flavinos s) exposed by angular stomatitis with fissuring (cheilosis) seborrhœa acne rosacea possibly interstitial keratitis—signs associated with pellagra

Summary —Pellagra due to ill balanced diet can be prevented by suitable dietary alterations and by addition of vitamin B_2 complex

PATHOLOGY

Main features often obscured by co-existing disease especially bacillary dysentery and tuberculosis General atrophy emaciation deep pigmentation of viscera brown atrophy of heart atrophic changes in suprarenals some atrophy of brain distension of lateral ventricles degeneration of lateral columns and crossed pyramidal tracts of cord atrophy of anterior cornual cells

Microscopic changes —Chromatolysis and disappearance of Nissl s granules in posterior spinal ganglia marked chromatolysis of Clarke s columns Betz cells of cortex and Purkinje cells Resemblance to central neuritis and subacute combined degeneration of cord No changes in C S F

CLINICAL FEATURES

Prolonged course Note regular periods of quiescence and exacer bation May last for years Diagnostic triad—*dermatitis diarrhœa dementia*

Prepellagrous symptoms (larval pellagra) —Frequent and may escape detection stomatitis raw red tongue as in sprue with angular stomatitis atrophic scaly lips (*perleche*) bleeding swollen gums conjunctivitis with lacrymation seborrhœic excrescences on naso labial folds alæ nasi and bridge of nose Roughened skin over knees and elbows *phrynoderma* or toad skin Often no further symptoms noted

Digestive symptoms—Nausea vomiting flatulence diarrhœa often steatorrhœa resembling sprue meteorism + Epigastric and abdominal tenderness

General appearances—Tense staring look irritable stupid morose headache pains in loins and back

Skin symptoms—Dermatitis may be earliest symptom noted but is usually secondary to general metabolic disturbance symmetrical, characteristic erythema like sunburn on exposed parts back of hands dorsum of feet forearms chest neck face (butterfly patch) and usually on scrotum or female genitalia symmetrical patches behind mastoid processes spreading downwards round neck like collar (Casal s necklace) Areas affected are tense swollen burn and itch on exposure to sun petechiæ bullæ and fissures common After 14 days desquamation hyperkeratinization roughened sepia pigmented skin which gives the condition its name *pelle* (skin) *agra* (rough) Atrophy of intrinsic muscles of hands is common causing a wrinkled appearance (washer women s fingers) colour of skin naturally varies in different races—blackish purple in negroes Burning sensation of feet and hands possibly due to liberation of histamine Local œdema of legs and generalized anasarca not uncommon in acute cases With each recurrence of dermatitis pigmentation is increased

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Prophylaxis —Mainly improvement in dietetic standards Maize flour as standard diet prohibited

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TROPICAL SPRUE (Psilosis Ceylon Sore Mouth)

(P A = Pernicious anæmia HCl = Hydrochloric acid)

Syndrome glossitis emaciation megalocytic anæmia steatorrhœa of long duration in tropical countries Resembles idiopathic steatorrhœa sometimes known as non tropical sprue also cœliac disease in children

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

Particularly in India and S China Ceylon Philippines Mauritius N Australia rarely in Pacific Islands Central Asia (Transcaspia) W Indies (Porto Rico) South U S A Central and S America Rarely in N Africa Palestine Syria and S Italy Apparently absent from Central Africa Sometimes has seasonal incidence In India and Ceylon at 6,000 ft

Europeans especially liable but may occur in Indians especially those who have adopted European life rare in indigenous natives almost unknown in negroes Chinese and Japanese liable

Both sexes equally liable in third and fourth decade unknown in small children (youngest reported 11) not common in young adults Husband and wife may be attacked at same time

Popular theory in Ceylon and India of association with housing—sprue bungalows (dry rot in walls) but no universal connection

ÆTIOLOGY

Initial cause still obscure Remarkable characteristics

(1) **Latency** may commence 25 years or even longer after quitting endemic area

(2) **Remissions** disease may recur 20 years or more after initial attack

(3) **Long residence** in endemic area formerly considered necessary (2–3 years or more) In recent war in Burma from 1942–1945 sprue behaved like epidemic disease with a short incubation period in some instances two weeks Sprue appeared on an unprecedented scale in widely separated areas—unconnected with dietetic or climatic factors There it observed distinct regional distribution though confined to India and Burma It was absent amongst troops in the Pacific combat zone Three quarters of the cases had less than two years service In 1944 some 675 British soldiers were invalided to England with sprue Seasonal incidence in E India lasted from March to September but peak incidence in June which corresponded with the fly season and outbreaks of bacillary dysentery

Possibly to fit in with all peculiarities sprue may be virus infection Dietetic cause suggested but difficult to prove Sprue syndrome is expression of chronic jejuno ileal insufficiency (Bennett) Main signs and symptoms common to other diseases in which there is damage to absorptive surface of small intestine Interference with normal absorption of proteins sugar and especially of fats Mechanism of fat absorption probably same as in cœliac disease and idiopathic steatorrhœa

N B —Several factors are common to sprue pellagra and P A they may merge into one another therefore border line cases occur

PATHOLOGY

Skin dry rough lemon yellow Emaciation + absence of sub cutaneous and omental fat Atrophy of liver + sometimes fatty degeneration Heart brown atrophy Diaphanous distended small intestine many changes formerly described due to post mortem changes Discrepancy in different accounts Generally considered that villi are shrunken atrophied with subacute inflammatory changes and sometimes ulceration Mesenteric glands enlarged and fibrotic Bone marrow hyperplasia as in pernicious anæmia Death usually from intestinal atrophy anæmia perforation of ileum

Clinical pathology

Fæces steatorrhœa large copious acid sour odour contain bile 5 times normal size excess of fat 50 per cent or more colour masked by fat and alteration of bile pigments excess of fatty acids three times that of neutral fat fatty acid crystals and fat droplets seen in microscopic preparations Indications that pan creatic function is normal fat is split but not absorbed *Low* fat content of blood (412 8 mg per cent —normal 600 mg per cent) Sigmoidoscopy shows rosy red injection of intestinal mucosa

Urine in acute stage urobilin + coproporphyrinuria indican

Gastric juice usually hypochlorhydria in cases with severe anæmia achylia gastrica (unlike pernicious anæmia HCl returns under successful treatment) Gastroscopy shows atrophy of gastric mucosa as in P A

Blood anæmia pronounced usually megalocytic with anisocytosis and polychromasia normoblasts rare Colour index above 1 (as in P A) Most severe anæmia in elderly patient *Hæmolytic* crises not uncommon Hyperbilirubinæmia usual though not as high as in P A Price Jones curve as in P A Hypocalcæmia in well marked cases (8–9 per cent normal 11) Hypocholesterol æmia Flat blood sugar curve (as in idiopathic steatorrhœa)

Explanation of steatorrhœa (mechanism of fat absorption) —Possibly result of functional pathology of absorptive surface of villi Primary cause may be abnormal gastric function

CLINICAL FEATURES

Great variability Usually chronic and intermittent may last 10–15 years or longer Three cardinal symptoms glossitis meteorism diarrhœa Diarrhœa in early morning sometimes nocturnal Meteorism excessive after food especially at night

Secondary sprue —Not infrequent sequel to other intestinal diseases such as bacillary or amœbic dysentery often after malaria In women during pregnancy or parturition

Mouth symptoms —Usually precede diarrhœa—not *always* Not in variably present Sometimes noticed for a year before diarrhœa Glossitis v painful accompanied by taste *loss* and *often* by salivation in extreme cases by angular stomatitis (as in pellagra) varies from day to day Extremely sensitive especially to salts

and acids Frequently evanescent aphthæ on tip or under surface of tongue lower lip and buccal mucosa Glossitis aggravated during exacerbations Inflammation of fungiform papillæ atrophy of filiform *Larval or presprue glossitis* may precede fully developed syndrome

Dyspepsia —Epigastric oppression, gaseous distension after meals borborygmi

Dysphagia —Œsophageal pain not uncommon especially in anæmic patients

Tetany and cramps —In longstanding cases (hypocalcæmia) Trousseau s and Chvostek s sign occasionally

Diarrhœa —Acute in early stages usually early morning diarrhœa may be watery frothy copious containing undigested particles but always offensive and accompanied by flatulence + Excoriation of anus not uncommon in women pruritus vaginæ also

Temperament — Spruey —unreasonable and irritable Longstanding cases may be partially demented *Memory defective* loss of powers of concentration Dusky pigmentation of skin not infrequent In women usually amenorrhœa

Types —*Gastric* —Glossitis gastric oppression and distension no diarrhœa but large fatty stools

Intestinal —Diarrhœa and fatty stools emaciation and anæmia glossitis *absent or may appear as terminal phenomenon*

Mild —Steatorrhœa without diarrhœa slight anæmia no emaciation

Sequelæ —Severe anæmia *resembling* P A *frequent* sequel after apparent recovery may sometimes be difficult except by achylia gastrica to differentiate from P A

Subacute combined degeneration of cord very rare

Other avitaminoses scorbutic symptoms occasionally tingling and paræsthesia with loss of reflexes (avitaminosis B_1) ariboflavinosis

Œdema of extremities not uncommon probably nutritional

Dermatitis not uncommon sometimes definitely pellagrous

Secondary sprue —Sprue symptoms secondary to bacillary or amœbic dysentery or often intestinal disease especially hill diarrhœa (*q v*)

Mortality —Now small (1 5 per cent) Death from asthenia severe anæmia sometimes perforation of ileum rarely thrombosis of mesenteric veins

DIAGNOSIS

On clinical appearances especially on analysis of fæces and megalocytic anæmia Note *absence of osteoporosis*

Differential diagnosis —From *cœliac disease* resembles sprue but always in infants Glossitis not usually present

Idiopathic steatorrhœa Probably cœliac disease in adult life skeletal changes *osteoporosis* infantilism megacolon clubbed fingers brittle nails lens opacities fine silky hair glossitis usually (but not so marked as in sprue) anæmia variable usually not severe usually hypochromic Does not react so favourably to treatment with folic acid and liver extracts

Pancreatitis —Alkaline fatty stool free fat is in excess of neutral fat and soaps

From P A —Not always easy achylia gastrica without response to histamine No steatorrhœa

Sometimes from *Addison s Disease* (low B P)

Gastrojejuno colic fistula malignant disease of *mesenteric glands* and tabes mesenterica may simulate sprue

TREATMENT

Removal from endemic area essential Sprue cases do not do well in heat Improvement on voyage to England usual Bodily and mental rest essential Strict bed till diarrhœa ceases In cold climate patient must be kept warm Nursing important Stools weighed daily *Diet very important* high protein diet with liver and minced meat Milk no longer considered a cure but where assimilation is grossly impaired and glossitis is acute specially prepared Sprulac * is beneficial Small quantities at frequent intervals Convalescent diet important fats and starches carefully controlled Fruit advantageous especially bananas and strawberries

Specific treatment —Folic acid (folvite) should be commenced directly *diagnosis is made Effects first seen on glossitis and mouth* symptoms Appetite improves and diarrhœa abates Weight increases Dose for adult 30 mgm daily for 10 days 20 mgm for an equal period and thereafter 5 mgm daily as maintenance dose In order to prevent neurological manifestations folic acid must be combined with liver therapy *Thymine (5 methyluracil) in doses* of 6 gm daily for 14 days may be substituted also teropterin

Medicinal treatment —For diarrhœa collosal kaolin sulphonamides —sulphasuccidine

For meteorism injection of pitressin ½–1 c c Small doses of ol ricini

For glossitis glauramine (acriflavine mouth wash) For angular stomatitis riboflavin 3 mgm daily

For anæmia liver injections in large amounts 4 c c alternate days for severe cases for 12 injections most efficient preparations *campolon anahæmin hepatex examen* Vitamin B_{12} *(y'amen)* 15 µmg injected intramuscularly twice weekly (1 c c) is followed by *rapid hæmatological response* In extreme cases blood transfusion most beneficial Reservoir dosage of liver extract 2 c c weekly during convalescence

For dyspepsia acid hydrochlor dil 20–30 min (1 2–1 8 c c) t d s

Progress —Folic acid 5 mgm daily for 6 months plus liver injections Effects of modern treatment very *good Cessation of* diarrhœa improvement in colour and size of stools increase of *weight* Improvement of blood Severe cases recover in 1–2 months

Prognosis —Good under present conditions and after prompt removal from tropics Return to tropics inadvisable before a year at *least* free from symptoms Relapses likely especially if over 50 years *in extremes of climate* hot or cold

* From " Cow and Gate Ltd. also chemists

HILL DIARRHŒA

Resembles incipient sprue and regarded as initial stage of it In Europeans at high altitudes (above 6 000 ft) in Himalayas also said to occur in S Africa and S America but doubtful Liquid offensive steatorrhœa as in sprue meteorism and flatul nce No glossitis or stomatitis Abates usually on removal from endemic area but may merge into sprue Has been ascribed to abdom nal chill, mica in water and other causes True ætiology still obscure

Treatment.—Hydrochloric acid and pepsin mixtures Probably also reacts to folic acid

CHAPTER VIII

CLIMATIC DISEASES

HEAT STROKE, THE EFFECTS OF HEAT

Moist heat most important air temperature wind velocity and relative humidity also contribute In calm air human body can support air temperature of 100 F if relative humidity is less than 90 per cent 120 F if humidity less than 40 per cent 140 F if humidity less than 15 per cent Death occurs at 128 F with wind velocity of 20 miles per hour at 117° F with wind velocity of 56 miles per hour

I HEAT EXHAUSTION

Faintness is brought on by exposure to high atmospheric tempera ture Collapse is attributable to physical exertion in hot environment in absence of salt deficiency Symptoms and signs similar to those after exertion in ordinary environment but relatively more severe Exertion is stopped at stage of exhaustion but collapse may occur taking the form of syncope

Salt deficiency heat exhaustion and collapse—Attributable to in adequate replacement of salt loss in hot environment leading to dehydration and oligæmia Symptoms and signs are similar to hypochloræmia under ordinary conditions For prevention increase salt intake to 28 gm (1 oz) daily Fluid up to 16 pints May be chronic with asthenia or acute with collapse pallor sweating vomiting and sometimes muscle cramps Urine scanty concentrated free from chlorides Hæmoglobin concentration and plasma protein raised Relieved by re toration of blood chlorides

Water deficiency heat exhaustion and *collapse*—*Attributable purely* to lack of drinking water in hot environments Thirst discomfort anorexia weariness eventually dyspnœa and cynosis Finally inability to stand erect restlessness and dilirium Relieved by water replacement

Anhidrotic heat exhaustion and collapse—Attributable to chronic sweating deficiency Associated with or preceded by severe prickly heat and skin changes—*Miliaria profunda* Symptoms may be present when at rest if area of sweating deficiency is large or heat very great Aggravated by exertion General mental and physical asthenia difficulty in concentration and in sleeping *Eventually collapse with loss of consciousness* After exposure to heat stress skin is dry except on face palms soles and axillæ Slow to return to normal sweating

Heat cramps (Miners cramp Stokers cramp)—Attributable to salt deficiency in hot environment Painful spasms of voluntary muscles usually *following activity and precipitated by drinking* unsalted water Relieved by administration of salt

Sunburn—Attributable to exposure to sunlight Acute erythema if extensive may cause malaise headache fever and occasionally *vomiting May interfere with heat regulation when affected* areas lose vasomotor control and do not sweat

Prickly heat (Miliaria rubra)—Attributable to extensive sweating accompanied by prickling (see p 168) Generalized anhidrosis may follow prickly heat

Acute heat neurasthenia—Attributable to short term exposure to hot environment in absence of salt water or sweating deficiencies Symptoms of fatigue tiredness disinclination to work irritability Partly attributable to inadequate adaptation of circulatory system

Chronic heat neurasthenia—May simulate effort syndrome Loss of energy initiative and interest Loss of weight and appetite fall in standard of performance Symptoms relieved after removal from environment

Heat œdema—Attributable to alteration in vasomotor system during acclimatization to heat Œdema of extremities especially ankles May produce incapacitating swelling Usually transient

II HEAT HYPERPYREXIA

(Heat stroke Siriasis)

It is an acute condition in high atmospheric temperature with hyperpyrexia *coma and pulmonary œdema* Heat hyperpyrexia is an exaggeration of heat exhaustion

Geographical distribution and epidemiology—Restricted endemic *areas In America* in summer in big towns on East Coast Mississippi Valley Gulf of Mexico Amazon and La Plata Valleys in S America *In Africa the Nile Valley* coasts of Red Sea Algeria Syria Iraq In India valleys of Indus and Ganges Lower Burma Tonquin S E China *In Australia Murray* River Queensland Coast Usually when atmospheric temperature is from 120–130° F in shade

Ætiology.—Europeans especially newcomers more liable than natives or longstanding residents All ages and both sexes are liable men more than women on account of their habits Attributable to failure of heat regulating mechanism peripheral or central may occur following known generalized anhidrosis Atmospheric heat on body overheating of blood auto intoxication indican acetone and diacetic acid in urine Suppression of sweat precedes onset of serious symptoms exhaustion of sweat apparatus Skin hot and dry

Hypodermic injections of atropine predispose to heat stroke

Pathology.—Rigor mortis early Blood fluid congestion of venous system and right side of heart blood and muscles acid in reaction Heart in rigor mortis contraction of left ventricle Venous congestion of meninges necrotic changes in ganglion cells of brain with chromatolysis of nuclei Cerebrospinal fluid and pressure increased Intestinal mucosa swollen and congested Temperature of cadaver rises after death to 114° F

Clinical features.—Heat hyperpyrexia develops independently of exposure to sun often during night pains in limbs vertigo headache mental confusion anorexia thirst photophobia chromatic aberrations of vision suffused eyes vomiting suppression of sweat urinary irritability loss of knee jerks Then restlessness wild delirium coma hyperpyrexia (to 110 F 43 3 C) Pupils contracted deep reflexes absent diarrhœa + skin emanates mousy odour urine often shows red blood corpuscles albumin and casts

Dehydration of blood with concentration of hæmoglobin to 110 polycythæmia and leucocytosis diminution of blood chlorides and plasma bicarbonate rise in lactic acid blood sugar and urea Hypochloræmia seen by low urinary chlorides

Test.—To 5 c c urine in test tube add 5 drops concentrated nitric acid and a few drops of 1 per cent solution of silver nitrate A slight haze or no change in solution shows absence of chlorides May also contain sugar and acetone and sometimes diacetic acid albumin and hyaline casts

Three types —

1 GASTRIC.—Gastric symptoms predominate vomiting epigastric pain Axillary temperature normal rectal temperature raised

2 CHOLERAIC.—Sudden onset diarrhœa resembling true cholera Rectal temperature 110 F

3 TRUE HEAT HYPERPYREXIA.—Nervous symptoms predominate accounts for 70 per cent of cases

Death occurs within a few hours from coma due to *respiratory failure* Recovery often followed by relapse In favourable cases terminates by crisis and rapid convalescence Mild cases usually in majority in them the painful cramps form a valuable diagnostic sign.

Anhidrotic heat exhaustion and collapse—Attributable to chronic sweating deficiency Associated with or preceded by severe prickly heat and skin changes—*Miliaria profunda* Symptoms may be present when at rest if area of sweating deficiency is large or heat very great Aggravated by exertion General mental and physical asthenia difficulty in concentration and in sleeping Eventually collapse with loss of consciousness After exposure to heat stress skin is dry except on face palms soles and axillæ Slow to return to normal sweating

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Diagnosis and differential diagnosis—Hyperpyrexia distinctive Differentiate from uræmia diabetic coma alcohol opium carbon monoxide and hydrogen sulphide poisoning may simulate cerebral or pontine hæmorrhage Diagnosis from cerebral malaria difficult because heat hyperpyrexia is more common in malarial subjects rely on enlargement of spleen history and parasites in blood (these may be scanty) Often mistaken for cerebrospinal fever distinguish by refractory irregular pupils strabismus Kernig s sign herpes and initial rigor

Treatment—In hyperpyrexia if malaria suspected quinine should be injected intravenously 7–10 gr (470–648 mgm) of quinine dihydrochloride Every effort must be made to reduce temperature patient placed on wet sheet bed cradles or rush covered bed (angareeb —Arabic) Continuous ice water spray with electric fan stimulates sweating In Iraq in second world war continuous drip saline intravenously gave best results For convulsions and restlessness potassium bromide or chloral Rubbing skin with ice obstructs evaporation and is not recommended Keep thermometer in rectum and discontinue application of cold at 104 F (40° C) If carried beyond this point temperature may sink to 91° F and dangerous collapse ensue Patient is then wrapped in dry blanket and stimulants given—tinct digitalis min 40 For convulsions venesection For respiratory involvement apply artificial respiration Lumbar puncture for cerebral cases Gastric cases sodi bicarb 30 gr (1 9 gm) every two hours During convalescence patient should be shielded from heat as sweating is not restored for 3 weeks

Prophylaxis—Patients in hospital with malaria typhoid etc are especially liable to heat stroke Suspect those with urinary irritability and suppression of sweat Salt valuable prophylactic (see below) Heat stroke huts and wards are now provided—air conditioned wherever possible—and methyl chloride or ammonia refrigerating machines employed Improvised cooling apparatus can be made by filling radiator of lorry with ice and driving fan forcing air by means of a tunnel into a one bedded bunk Return to hot climate should be prohibited as otherwise relapse will occur

Acclimatization—*Now practised* in S Africa for work in mines candidates are tested in special room at 94° F (34 5° C) wet bulb temperature and then graded according to reactions and ability *to sweat Men born* and bred in hot climates do best Water *consumption necessary* in endemic area allowance should be 3 gallons (11 3 litres) of water per man at work with addition of ½ oz (15 7 gm) salt to each gallon (3 7 litres) to counteract hypochloræmia

LÂTAH—RUNNING AMOK—KORO

Name signifies nervous or sensitive state— *Young dah hte* Common in Malaya Java Dutch E Indies Frequently in young women Psychotic state lasts for years but does not lead to insanity

Latah Individual reacts involuntarily to stimuli by irritating words or gestures During hypnotic state is sensitive to suggestions High degrees may be followed by swooning and exhaustion Latah individual will imitate pedalling of bicycle till exhausted etc in others sudden touch or auditory stimulus causing jump or recoil Hereditary tendency to latah in every Malay

Amok —Insensate fury driving victim to kill without reason—generally brooding upon imaginary grievance—most common in Malays drugs like Indian hemp (*Cannabis indica*) predispose

Koro —In Macassar Celebes and S China denotes shrivelling feeling of penis retracting into abdomen Patient may die Anxiety neurosis grasps penis and begs for assistance In anxiety will tie penis to leg or anchor it by string Pathological conditions such as oedema of abdomen hernia hydrocele or elephantiasis of scrotum may evoke attack

Other hysterical states in natives — *Banza* on Congo in women at puberty etc

TROPICAL NEURASTHENIA

Neurasthenia in tropics does not differ essentially from similar condition elsewhere but is usually more marked and commoner Tropical conditions provoke manifestations in predisposed individuals Possibly a certain number go to tropics to escape strain of social life at home Predisposing causes chronic malaria dysentery etc isolation heat insect bites disturbed sleep proximity to natives with undue appreciation of their psychology Aggravating factors absence of seasonal changes monotony and unpalatability of diet Tropical heat engenders insomnia which at end of tour causes psychoneurosis In women menstrual disturbances parturition changes and anxiety neurosis are common Tropical climate is at first exhilarating but becomes depressing Hyperglycaemia may possibly be caused by heat precipitating factor

Clinical features —Patient becomes emotional and introspective with tremors sweating palms abdominal sensations and exaggerated deep reflexes Sometimes there is divergence of pupil on accommodation (Moebius sign) Sometimes a suggestion of hyperthyroidism

Treatment —Most recover on removal from tropical surroundings but illness may be prolonged Remove underlying cause—malaria for instance ancylostomiasis or amoebic dysentery Holiday in temperate or cool climate Encourage hobbies and interests Sedative mixtures bromides For insomnia luminal or allonal

Prophylaxis —Subjects of profound neurasthenia should not be permitted to return to tropics relapse probable Sometimes recovery may be complete but at least six months rest is usually necessary

PRICKLY HEAT

Miliaria with excessive sweating and principal factor in heat stroke in all tropical climates

Ætiology—Mechanism probably depends on cells of stratum corneum which swell and obstruct orifices of sweat glands Yeasts and mycelium (*Oidium*) frequently in contents probably secondary invasion Miliary rash commonly known as prickly heat is due to dysfunction of the small sweat glands and pemphigoid eruption due to similar condition of the large sweat glands and may be associated with heat exhaustion Four types —*Miliaria rubra*—papulovesicular dermatitis connected with hyperhidrosis may result from few occluded glands in ante cubital popliteal fossæ chest and abdomen *Miliaria pustulosa*—numerous pustules unassociated with hair follicles Purulent exudate associated with *Staph albus* *Miliaria profunda* associated with tropical anhidrotic asthenia *Miliaria crystallina* superficial transient rash causing little discomfort

Clinical features—Every European liable especially newcomers Some never get acclimatized but disease recurs every year in hot season Miliaria like eruption small vesicles and closely set red papules—impression of skin sprinkled with grains of sand—mostly on apposing surfaces where subjected to pressure by clothes —under breasts mid abdomen axillæ sometimes also backs of hands forehead scalp palms escape Interferes with sleep may lead to boils Prickling and itching provoked by drinking hot fluids Exposure to sun close rooms and warm clothing aggravate

Treatment—Avoid cause of perspiration hot fluids exercise and especially soap in bath Mattress and pillows should be covered with grass mat Punkah or electric fan by night Afridol soap (oxymercuriotoluylate of sodium) is preventative and curative Powder body—axillæ and crutch—with astringent powder (equal parts boric acid zinc oxide and starch) Flannel shirts are better than cotton To intractable patches apply calamine lotion or powder of sublimed sulphur 80 magnesia 15 oxide of zinc 5 parts Recently established that prickly heat is relieved by reducing salt intake so that relapse can be brought about by increasing intake of salt Relief from symptoms produced by pyribenzamine a histamine preparation

Prophylaxis—Inunction of skin with lanoline once weekly recommended Also Caladryl ointment

TROPICAL CHEIROPOMPHOLYX

Vesicular eruption on hands fingers and feet Common in Africa and India Probably eczematous aggravated by heat Owing to thickness of horny layer vesicles remain in skin for days and become secondarily infected Some forms are caused by external irritants or toxic eruptions due to ringworm

Treatment.—Calamine and lead lotion with *Liq picis carbonis* Also ointment of coal tar 3 powdered charcoal, 1 zinc oxide 1 lanoline and petroleum jelly 12 parts The ointment is well rubbed in and cotton gloves and socks worn Resorcin soap is helpful

CRAW CRAW NODULAR DERMATITIS

Papulo pustular skin affection common in Central Africa Ceylon India S China Commences as itching papule which becomes generalized on back chest arms Mostly climatic but many cases are probably pustular scabies or nodular dermatitis associated with *Onchocerca volvulus*

Treatment.—Pustules opened crusts removed ulcers scraped and dusted with boric acid powder washed with corrosive sublimate lotion (1 1 000) covered with absorbent cotton wool and bandage Penicillin ointment or injections

CHAPTER IX

MISCELLANEOUS GROUP

AINHUM

Fibrous constriction of toes especially 5th sometimes little finger Rare in women and children chiefly in adult male natives of E Indies and other indigines especially negroes Africa and America

Commences as narrow groove in skin on plantar side of little toe gradually involves circumference constricted as by ligature one or both feet affected No pain toe drops off or is amputated Third and fourth toes rarely affected big toe never occasionally 5th digit of hand Osteoporosis and atrophy of bone Only treatment effective is amputation

BIG HEEL

Epidemic hypertrophy of os calcis in natives of W Africa (Gold Coast) and in Formosa in young adult males Fever pain swelling of os calcis and occasionally other tarsal bones

ONYALAI (Essential Thrombocytopenia)

In natives of E Africa Rhodesia Congo possibly also in China Bullous sanguineous vesicles ½–¾ in (1 25–1 8 cm) on hard palate and buccal mucosa Hæmaturia numbness tingling and pain usually parotitis and mental convusion Pyrexia 103–104 F (39 4–40 C) May be widespread hæmorrhages epistaxis subconjunctival hæmorrhages Death from hæmorrhagic bronchopneumonia Non infectious familial Blood great reduction in platelets Considered to be essential thrombocytopenia due to defective nutrition *Differential diagnosis* from snake bite

Treatment.—Blood transfusion combined with autohæmotherapy

TROPICAL EOSINOPHILIA

(Pulmonary Eosinophilosis)

First described as pseudotuberculosis of lungs associated with massive eosinophilia in India but widely diffused in tropics—India Africa China Philippines S U S A Spasmodic bronchitis leucocytosis of 60 000 *with high eosinophilia* up to 90 per cent—higher than in any disease except eosinophilic leukæmia Males affected more commonly than females Febrile periods with splenomegaly Acute and chronic types recognized X rays show disseminated discrete mottlings with average single focus about size of split pea somewhat resembling silicosis

Ætiology—Circumstantial evidence of virus occurring in groups or families spread by fæces under insanitary conditions Helminthic allergy suggested by recent work

Pathology essentially eosinophilic bronchitis and bronchiolitis Reddish brown areas scattered on surface of lungs with tubercle like nodules *composed of giant cells and monocytes* *In serum cold agglutinins* (isoagglutinins) are present in high titre The disease is usually benign and lasts for years and tends to observe a seasonal incidence Tropical eosinophilia has to be distinguished from Löffler s syndrome which is an allergic manifestation resembling tuber culosis from pulmonary coccidiomycosis sarcoidosis and bronchial asthma associated with periarteritis nodosa

Diagnosis by eosinophilia *Distinguish from parasitic eosinophilia by* A C T H or cortisone in divided doses in 1–2 weeks No effect on latter rise of eosinophiles in allergic conditions (Thorn test)

Treatment—Arsenic in some form or other is specific and reacts quickly to intravenous injections of neoarsphenamine in courses of six doses of 0 15 to 0 45 gm Mapharside neohalarsine acetyl arsan (stovarsol) also effective Benylin expectorant relieves bronchial spasms
Recent discovery of specific action of hetrazan 600 mg daily for 4 days reduces eosinophilia to normal from 5th day onwards Pul monary signs and symptoms also clear up (Danaraj 1956)

CHIUFA

Gangrenous rectitis *In N Rhodesia at 200–2 500 ft Onset* sudden and acute Circum anal skin and vulva have white powdery appearance *Generalized pains T 104 F Rectal prolapse* tenesmus rectal distress at first no diarrhœa but usually constipation Later in flammation spreads to colon and there is then diarrhœa Similar affection of vagina reported

ULCUS TROPICUM (Tropical sloughing phagedæna)

A particularly destructive form of ulceration of legs ear and rarely other parts especially in debilitated natives

Geographical distribution and epidemiology.—In most tropical countries with hot moist climates commonest cause of sickness in W E and C Africa India Malaya Pacific Islands S America Majority of ulcers occur during period of low rainfall and low relative humidity

Ætiology.—True ætiology obscure many organisms in slough but probably has nutritional basis spirochætes common *Sp schaudinni* but true infective agent not isolated may be ultra microscopic but sores have been reproduced by inoculation Commences at site of previous abrasion—insect bite or scar of healed ulcer often on yaws gumma or crushing or bruising injury—on ankle and tibial area especially because most exposed to injury but may occur on arms or hand Biochemical deficiencies urged as predisposing cause but may occur in otherwise healthy Europeans in endemic areas Hypocalcæmia low blood sugar and low blood urea Diet deficiencies especially protein B_2 and A predispose Commonly associated with chronic malaria Virulence of virus appears increased by continued transmission in susceptible community In Mohammedan countries liable to occur during Ramadan

Clinical features.—Commences as papule or bulla with serous sanguinolent contents pain + and some constitutional disturbance Bulla ruptures ashy grey moist slough involves subcutaneous fascia centre liquefies and involves fascia muscles periosteum and bone Generally process is limited and superficial but in advanced cases joints tendons and blood vessels are destroyed necessitating amputation Frequently also septicæmia and death

Diagnosis and differential diagnosis.—By appearance malignant character and punched-out edge From yaws and syphilitic ulceration varicose ulcers oriental sore and veld sore

Treatment.—Diet essential—fruit vegetables limes oranges fats and butter (vitamin A) Cod liver oil dressings in early stage when localized excision and skin grafting When septic and ulcerated scraping is necessary followed by swabbing with alcohol and strapping with elastoplast *Copper sulphate treatment*.—Copper sulphate 1 oz (31 gm) glycerin 2 oz (59 1 c c) heated and stirred acid carbolic 1 drachm (3 55 c c) to every oz of solution Ulcer is cleansed and solution applied on cotton wool for 2–3 min Dressing of acriflavin (1 1 000) on gauze covered with hot fomentation Tar treatment much employed in Kenya ulcer swabbed with eusol tar spread on lint changed every 2–3 days Small ulcers dressed with iodoform gauze and elastoplast dressing Sulphonamides recently used in Trinidad Sulphapyridine 3 gm (46 2 gr) daily by mouth is useful in papular stage but not in chronic Sulphonamide paste is effective in cleansing up septic edges (Sulphonamide P (B D H) contains 30 per cent sulphonamide in cod liver oil base) Penicillin injections in large doses generally recommended Peri arterial lumbar sympathectomy has been performed

LEUCODERMA (Vitiligo)

Atrophied depigmentation areas of skin extremely common in native races almost any part of body affected Patches enlarge peripherally observing certain rough symmetry Texture and glands of skin un affected Generally considered to be a *trophoneurosis* Cases with positive W R may be syphilitic in origin and improve with anti syphilitic treatment Popularly mistaken for leprosy In Calcutta *Bouchi oil* injections are employed extracted from seeds of *Psoralia comyfolia* Injections of 0 05–1 c c into patches number of injections varying with size of patch Formation of pigment noted after 2–3 weeks

CHAPTER X

VEGETABLE POISONS

LATHYRISM —FAVISM

Abyssinia Algeria and India principally Nervous manifestations ataxy spastic paraplegia weakness muscular pains wherever vetches form main articles of food Formerly Khasari —*Lathyrus sativus*— suspected but now shown that seeds of *Vicia sativa* var *angustifolia* contain alkaloids—*vicine divicine* This vetch found also contamina ting wheat in India Disease reproduced in animals on same diet Arms and trunk seldom involved incontinence of urine sexual im potence common and early chronic seldom fatal Aneurin (vitamin B_1) said to be effective in treatment

Favism is an allergic manifestation due to a bean (*Vicia fava*) and gives rise to a condition resembling blackwater fever Common in Sardinia Greece and the Mediterranean

ATRIPLICISM

China Combination of cutaneous and nervous symptoms Intoxica tion by ingestion of leaves of *Atriplex littoralis* also *A serrata* or *Chenopodium hybridum* Skin lesions light sensitive—itching of hands œdema and bullæ gangrene of finger tips cutaneous hæmorrhages Eyelids cyanotic and œdematous re embles Raynaud s disease or erythromelalgia

OTHER POISONS

ACKEE POISONING—VOMITING SICKNESS OF JAMAICA (ACUTE TOXIC HYPOGLYCÆMIA)

Jamaica (probably other W Indies) in circumscribed rural epidemics in cooler months November to April Considerable mortality Usually in children

Ætiology—Poisoning by Ackee—fruit of *Blighia sapida* a common tree When mature and in good condition fruit is wholesome but when injured on ground is poisonous Immature fruit contains a water soluble toxin Water in which fruit is boiled is most toxic Other vegetable constituents of bush teas are also under suspicion

Two polypeptides *hypoglycin* A and B have been extracted and identified from aqueous extract of seeds Both toxic to laboratory animals producing hypoglycæmia also characteristic of vomiting sickness and associated with fatty changes in liver and complete absence of glycogen The toxin produces a temporary enzyme block inhibiting gluconeogenesis The condition is in fact an acute toxic hypoglycæmia

Pathology—Hyperæmia with petechial hæmorrhages of viscera Fatty degeneration of liver kidneys sometimes pancreas and heart somewhat resembling yellow fever

Clinical features—Vomiting and abdominal pains then recovery but 3–4 hours later cerebral vomiting commences then convulsions and coma and death in 12 hours Convalescence rapid Mortality 80–90 per cent T subnormal rarely 101 F (38 3 C) Respirations rapid (26–30) of Cheyne Stokes type pupils dilated

Treatment—Prompt emetic wash out stomach with weak alcohol during primary vomiting

Prophylaxis—When fruit falls to ground only opened pods (ripe fruit) to be used for food Destroy immature pods

MANIOC

Manihot aipi (sweet cassava) and *M utilissima* (bitter cassava) Ground roots eaten as cassava cakes in W Indies

Poisoning from failure to remove glucoside and enzyme which with water release free hydrocyanic acid Causes vomiting abdominal distension and impeded respiration *Nami* (*Dioscorea hispida*) yams in Philippines cause similar symptoms

CORAL PLANT

Jatropha multifida causes colic cramps thirst and subnormal temperature *J curcas* and *J glandulifera* in W Indies nuts taste like almonds known as physic nuts *J gossypifolia* wild cassava or belly ache bush seeds intestinal irritant like croton oil *J urens* from same area bears leaves with stinging hairs which cause itching smarting flushing of face swelling of lips and faintness

JENGHOL POISONING

Java Bean *Pithecolobium lobatum* causes renal pain dysuria often anuria Urine shows blood-casts and sharp acid crystals which cause necrosis of urethra fistulæ and extravasation

characteristic a week after œdema erythematous on face rubeolar on trunks and limbs Vascular nævi with telangiectase may be nodular and bleed profusely usually form in three weeks may be sessile or pedunculated from pea to lemon in size Disturbances of heart and circulation frequent Lung sign characteristic—like bronchial spasm Urine of low specifi gravity Primary glaucoma often present

Diagnosis—On history œdema and peculiar rash From œdematou beriberi differentiated by pyrexia and persistence of deep reflexes From hunger or war œdema on clinical appearances and estima tion of serum albumin

Treatment—Egg and milk albumin administered in quantities Libera protein diet Tinct of ephedra 20–30 min with calcium lactate 10 gr tabs

IROKO ALLERGY

A number of dense hardwoods of tropical origins—satin wood teak and mahogany—are capable of causing allergic action in susceptible persons

Iroko—British standard trading name for wood of *Chlorophora excelsa* African teak imported in considerable quantities as substitute for real teak Wood dust produces irritation of exposed surfaces marked œdema of face with ocular irritation and blepharospasm acute coryza headaches and pharyngitis Certain soft woods especially *Obeche* (*Triplochiton scleroxylon*) also have a bad name

CATERPILLAR AND OTHER INSECT DERMATITIS

The hairs of species of caterpillar give rise to dermatitis and urticaria In New Guinea and N Australia it is the moth *Ochrogaster contraria* In Israel and the Middle East it is *Traumaleto pœa pinivora wilkinsoni* which occurs in the pines in afforestated areas Scales of adult moths which swarm round lights at night produce urticaria conjunctivitis and facial œdema In French Guiana the species is *Hylesia urticans* In French Equatorial Africa and the Gold Coast a similar species occurs in Brazil flannel moths (*Anaphe renata*) (*Megalopygidæ*) are well known In Celebes it is *Scirpophaga innotata* and in Japan large epidemics due to *Euproctis slava* have been recorded In Ecuador a greenish beetle (*Pæderus ornaticornis*) produces on contact a papulo-vesicular rash in the same manner as the blistering beetle *Lytta vesicatoria* or *cantharides*

BEE AND WASP STINGS

Numerous species in tropics give rise to painful stings and effects which are allergic are usually more intense than in temperate countries In Japan the bites of a parasitic wasp *Sclerodermus nipponensis* of which the female is ant like and wingless cause epidemics of pale swellings 10 mm in diameter leading to suppuration and lymphangitis

DERMATITIS VENENATA

Many plants cause dermatitis erythematous vesicular or urticarial Poison ivy (*Rhus toxicodendron*) poison sumac (*R vernix*) in N E U S A poison wood (*Metopium toxiferum*) in S W U S A produce severe dermatitis Contact with plant is necessary venom is *toxicodendrol* in small quantities 0 001 mgm Repeated attacks do not confer immunity

Treatment —Skin washed with soap and water do not apply alcoholic or oily solutions

Most plants are *more irritating* when wet Others causing dermatitis are *Cypripedium* lady slippers *Euphorbia* and primroses Lily and Vanilla bean rashes in Japan lacquer from *Rhus vernicifera* and sometimes lacrymation

Pyrethrum dermatitis in Kenya due to leaves of *Chrysanthemum cinerariaefolium* growing at high altitudes throughout the year—with pyrethrum content of 1–2 per cent Absorption facilitated by constant sweating Itching commences at corners of eyes followed by lacrymation

MUSHROOM POISONING

Poisonous species not recognized by taste have agreeable flavour Dangerous poisoning due to genus *Amanita* (*A muscaria* and *A phalloides* death cup) Both common and widely distributed in South U S A and S Europe Distinguished by persistence of portions of veil encircling stem and little below the cup Alkaloid *muscarine* allied to pilocarpine Atropine forms efficient antidote

Pathology —Congestion of internal organs subpericardial and subpleural hæmorrhages Liver intense fatty degeneration and necrosis (as in phosphorus poisoning) Kidney parenchymatous degeneration of convoluted tubules Severe and widespread damage in C N S Spores of fungi in fæces

Clinical features —*Gastro intestinal* nausea vomiting and diarrhœa *Choleraic* violent abdominal pain nausea vomiting with choleraic stools Severe hepatitis with jaundice Toxic nephritis anuria *Nervous* gastro intestinal symptoms followed by mental confusion and delirium in fatal cases *Rapid type* symptoms within three hours of ingestion *Delayed type* (*A phalloides*) 6–15 hours

Treatment.—Stomach pump as soon as possible Atropine in large doses intravenous salines Large doses of colloidal kaolin by mouth absorb muscarin

Death fish *Tetrodon hispidus* in Hawaii and other species in Japan and Korea have poison in ovaries and eggs producing severe gastro-intestinal symptoms King fish (*Scomberomorus cavalla*) an excellent fish is occasionally toxic

CLINICAL FEATURES

Pain extending up limbs profuse sweats pallor dyspnœa tachycardia vomiting diarrhœa morbilliform and scarlatiniform rash

TREATMENT

Local injection of 5 per cent pot permanganate + 2 per cent procaine + 1 1 000 adrenaline

For fish poisoning wash out stomach and give purgatives Combat shock with hot water bottles etc

Poisonous Shellfish—In S Pacific fatal cases of poisoning due to shellfish *Conus* all adorned with bright coloured shells *C tulipa C marmoreus C striatus C geographicus* and *C aulicus* Long tubular proboscis protruded beyond shell and opening into sac containing two rows of hollow teeth Poison delivered onto wounded surface Symptoms acute pain swelling numbness and paralysis—then drowsiness coma and death Incise and bleed Sometimes fatal in N Australia Polynesia and Seychelles

CORALS & SEA ANEMONES

Corals are formed of a number of cœlenterata and zoöantharia genus *Actinaria* Abrasions and cuts on skin cause indolent lesions Also sea anemones (in Mediterranean *Hellenopolypus* and *Aktinion*) give rise to sponge fishers disease Lassoo like tubular cells evert and end in harpoon like structure within few minutes of contact a small blister appears on skin like that due to cantharides irritates itches and is œdematous

Treatment—Apply vinegar and olive oil

JELLY FISH

Medusæ genus *Obelia* Certain *nematocysts* are weapons of offence ejecting barbs which have poisonous numbing effect producing local swelling urticaria and sometimes shock

Portuguese man o war *Physalia* has special stinging apparatus which produces dermatitis and skin irritation

SEA URCHINS (Echinoidea)

In West Indies especially Barbados spiny sea urchins cause septic lesions from punctures of hands and feet by spines *Tripneustes esculentus* and *Centrechinus antillarum* also have poisonous ovaries and spawn Pain nausea diarrhœa migraine resembling fish allergy also produced by Mediterranean species

Treatment—Spines are fragile and break off deeply Wounds dressed with antiseptic Tetanus antitoxin injected

SCORPIONS (Arachnida)

Scorpions common in tropics sting painfully but not usually dangerously except in children May cause death N and S Africa W Indies Mexico Korea Manchuria

Signs and symptoms—Local pain œdema cramps sweating pyrexia vomiting and convulsions In Trinidad glycosuria hyper glycæmia and pancreatitis reported as sequelæ Poisonous species—S Europe and N Africa—*Euscorpius italicus* *Buthus maurus* in S Africa *Hod enes* *Opisthophthalmus* and *Parabuthus* in Mexico species of *Centrurus* in Brazil *Tityus servatulus* in Manchuria *Buthus martensi* Paired poison glands in postanal segment of tail jointed and flexible Venom like cobra but less toxic

Treatment.—Incise sting wash with strong potassium permanganate solution For pain liq ammon fortis injection of novocain and adrenaline

Severe intoxication—Antitoxin prepared from venom extracted from dried sting and venom glands injected into horses 5 c c prophy lactic and curative

SPIDERS (Araneæ)

All possess poison glands Genus *Latrodectus* (widow spiders) toxic for man S Europe malmignatte (*L tredecimguttatus*) Palestine and Middle East *L lugubris* New Zealand *L hasselti* katipo N and S America *L mactans* and *L geometricus* In S Africa *L indistinctus* In Peru pruning spider *Glyptocranium gasteracanthoides* in S Africa Kroppie spider (*L indistinctus*) S Europe *Lycosa tarentula* tarantula hysterical disease in Middle Ages— tarantism Toxin of poison gland causes powerful hæmolysis hæmolysin causes œdema with numbness and urticaria nerve pain due to stimulation of myoneural junctions rigidity and spasm of abdomen board like resembling acute abdomen or appendicitis Sloughing of site of bite may occur In N Africa species *Chætopelma olivacea* feared by Arabs and bites give rise to acute inflammation

Treatment—Wash out wound with pot permanganate 1 4 000 and give by mouth Intravenous injection of calcium gluconate (10 c c of 10 per cent solution) relieves pain and muscular spasm Antiserum used in S Africa and Argentine

CENTIPEDES (Myriapoda)

Genus *Scolopendra* widely distributed in tropics poison apparatus at base of first pair of appendages in modified jaws *S morsitans* size 6 in venom causes local and general symptoms local œdema and lymphangitis dizziness headache vomiting

Treatment—Sol ammonia 1 5 morphia injections for pain

TICK PARALYSIS

Dermacentor andersoni wood tick of N America in E State *D variabilis* give rise by their bite to peculiar paraplegia in sheep also in man, sometimes fatal Similar condition in S Africa caused by *Hæmaphysalis cinnabarina* *Ixodes pilosus* in Australia by *I ricinu* and *I holocylus* Epileptiform convulsions in cats and dogs Poison introduced by tick during haustellation Wound painful with œdema and bleeding + in forcible removal of tick possibly due to an anti coagulin Symptoms suggest infantile paralysis *Quite distinct from* rickettsia disease To prevent onset of paralysis removal of tick must be complete as salivary glands are sources of toxin Protective serum introduced for treatment of dogs and has been successful in humans

CHAPTER XII

METAZOAL INFECTIONS

ARTHROPOD, FLY AND LEECH INFECTIONS

ARTHROPODA

ACARINE DERMATOSES

Several species of mite in grain sugar copra temporary parasites of skin causing intense irritation like scabies Grocer s itch due to *Glycophagus* in raw sugar erythematous rash Copra itch *Tyroglyphus* Grain itch *Pediculoides ventricosus*—cotton seed beans etc Severe pruritis papular urticarial rash *P ventricosus* usually parasitic on insects abdomen of female swollen with eggs like chigger Eggs hatch in abdomen young being small editions of adults

Nuñez Andrade disease—dermatitis from bites of larvæ of *Neoschon gastia nunezi* a common parasite of fowls produce small petechiæ Hæmatosiphoniasis in Mexico due to another fowl parasite—*Hæmato siphon inodora* (*Chinche de los gallos*) or the chicken bug

Harvest mites (*Trombidiidæ*) velvet mites adults bright red Velvet mites predaceous on insects and plants Larvæ (*microtrombidium or leptotrombicula*) harvest bugs =larvæ of *Trombicula autumnalis* and Chigger mite of U S A (*Eutrombicula batatas*) 150 μ long legs and body covered with feathered hairs Toxins injected by long suctorial tube formed by salivary secretions penetrates skin and digests surrounding tissues Other trombiculæ—transmit rickettsiæ of typhus Adults known as money spiders non parasitic Larvæ called Kedani mites —*Trombicula akamushi* *T schuffneri* *T deliensis* and *T hirsti* Inunction with oil of cajuput bandaging with subacetate

of lead or copper sulphate gives relief from intense itching. Infection with *d butyl phthalate* preventative and also a cure. Different species of harvest bugs in tropics are virulent especially in S Ginam (*Acarus balat*), New Guinea, Celebes (*Ms rotrowbi m a hmanni*), S America (*M m lelissmm m*) known as Bicho Colorado.

Demodex folliculorum in hair follicles and sebaceous glands; similar species in domestic animals. Minute (0 3–0 4 mm); causes seborrhoea and inflammation of Meibomian glands of eyelids. Abdomen separated from cephalothorax, elongated, transversely striated; head with prominent rostrum without eyes; mouth adapted for sucking; cephalothorax with 4 pairs of short rudimentary claws. To demonstrate, express sebum from sebaceous glands or comedones and examine with microscope in drop of xylol or oil. Lays heart shaped eggs 60–80 μ by 40–50 μ.

Sarcoptes scabiei itch mite causes scabies, particularly common in tropics; causes pustular rash especially in lepers like Norwegian scabies. In W Africa many cases of "craw craw" are scabies. Similar species in domestic animals, foxes, wolves, jackals and llama.

Female 0 3–0 4 mm, bigger than male (0 2 mm); sexes distinguished by epimera of second pair of hind legs which unite with sexual orifice in male and are free in female. Suckers on much reduced legs in female on 1st, 2nd and 4th legs in male. Surface covered with transverse folds and bears number of spines and conical scales. Gravid female lays eggs in skin; eggs measure 150 μ by 100 μ; in 3 5 days give rise to larvae and nymphs which live like adults and pass through 4 stages in 3 weeks. Nymphs moult, become sexually mature; average life of adult 4 5 weeks.

Treatment —Benzyl benzoate (*Proscabin*) lotion of equal parts benzyl benzoate industrial spirit soft soap—1½ oz. Treatment in 45 minutes, no damage to skin. Body washed with soft soap in warm bath at 100 F (38 C) for 10 minutes and brush. Second bath one day later. Simple treatment, rapid cure.

Rotenone —Active principle of derris root non-oily mucilaginous with 2 per cent rotenone. Twice daily for two days.

Tetraethylthiuram monosulphide in 5 per cent solution rubbed over body except on face and head twice daily; cheap, clean, effective.

Gammexane—½ per cent in ointment is said to be the most efficient remedy yet devised.

CHIGGERS —Chigger flea (*Tunga penetrans*) important as cause of suffering and invalidism. Imported from S America to West Indies, W and S Africa. More recently to E Africa and West Coast India. Somewhat like common flea, 1 mm long, large head, deeper brown abdomen. Lives in dry sandy soil—dust, ashes, stables and poultry yards. Attacks all animals and man. Lives free with male until impregnated, then burrows by mandibles into skin and ovulates; abdomen swells to size of small pea. Epithelial layer of skin becomes attenuated; parasite anchored in burrow by chitinous excrescences; spiracles project through opening. Eggs when mature are expelled through hole in skin.

female dies and parts slough away Larvæ hatch in soil in 3-4 days pupate on 6th imago emerges 17th day Chigger causes inflammation suppuration pea like elevations secondarily infected by pyogenic cocci or even by tetanus Feet commonly infected sometimes hands soles interdigital spaces roots of nails Usually one or two may be hundreds

Treatment —*Remove chiggers as soon as possible Kill by pricking* with needle chloroform turpentine or mercury ointment Enlarge opening by needle and enucleate chigger Antiseptic dressings

Prophylaxis —*Floors* swept and sprinkled with pyrethrum powder or carbolic acid cattle sheds and pigsties treated Pigs not kept in vicinity of houses High boots with powdered tobacco inside recommended Natives prevented from walking in bare feet. Daily inspection of feet also rubbed with mixture of lysol min 5 in 1 oz vaseline especially in interdigital clefts

LINGUATULIDÆ —Degenerate arachnids with annulated body roughly resembling tapeworms *L serrata* S Germany Switzerland Brazil Adult stage in nasal cavity of dogs wolves foxes sheep goats Larvæ in mesenteric glands of domestic animals Occasionally in liver of man Causes no symptoms Reported in Brazil as intestinal parasite Infection contracted by eating raw vegetables contaminated by nasal secretion of dogs

Body pear shaped flattened transversely striated with 90 rings *Male* white 18–20 mm by 3–5 mm *Female* 8–10 mm grey or brown packed with eggs Anteriorly 8–12 mm broad posterior 2 mm Eggs ovoid 90 by 70 μ Eggs with embryos deposited by female pass out with nasal mucus become attached to grass and ingested by definitive host penetrate mucosa and enter *viscera Larva (5–6 mm) encysts Ingested by carnivores* escaping from cyst falls into peritoneal cavity or even lumen of intestine and reaches adult stage in nasal cavity of same host

Porocephalus armillatus —Infests negroes in C Africa recorded from Java Sumatra Manila and China Adult form in trachea and lungs of pythons and snakes Nymphal form in lion mandrill giraffe African hedgehog Vermiform yellow translucent *Male* 3–5 cm with 16 rings *Female* 12 cm with 20 rings Eggs (80–100 μ) contain well developed larvæ Passed with bronchial secretion of snakes ingested with contaminated food or water by monkeys sometimes by man Egg envelope digested by duodenal (not by gastric) juice larvæ penetrate intestinal wall and peritoneum and enter thoracic or abdominal organs such as liver Protracted development (1–2 years) encyst as nymph When intermediate host is eaten by snake nymphs are liberated and penetrate into lungs where they develop rapidly into adult form Many cases found in Belgian Congo within lumen of small intestine and in lungs intus usception due to larvæ reported when cretified demonstrated by X rays

In Oriental region *P moniliformis* is parasitic in pythons—more slender more rings Two cases from U S A with *P crotali* of rattlesnake

Suggested that human infection is acquired from eating snakes but more probably by drinking water contaminated by snakes

MYIASIS

Partial parasitism by larvæ of muscid flies Eggs deposited on wounds or apertures in others larvæ emerge from hiding places to feed on blood

NASAL AURAL OCULAR MYIASIS

Cochliomyia hominivorax screw worm fly 9–10 mm long—America Canada to Patagonia Active in heat of day deposits 300–400 eggs in open wounds and in nasal cavities Larvæ screw worms hatch in a few hours destroy mucous membrane periosteum bone and penetrate brain—fatal Larvæ white 19 mm twelve segments and circles of spirally arranged spines Initial symptoms are tickling pains and nasal obstruction Epistaxis common

Chrysomyia bezziana—India and Cochin China breeds in living tissues producing destruction as above *Female* 8 mm by 13 mm metallic blue greenish thorax *Male* eyes reddish brown approximated Larvæ 12 mm yellowish white with pigmented extremities

Rhinœstrus purpureus (bot fly) — Head maggot Russia and N Africa Deposits eggs near the eye or nose Habits similar to bot fly of sheep

Wohlfahrtia magnifica (Russia and S Europe) — Flesh-eating fly breeds in living tissues especially wounds nasal fossæ palate and eyes 10–13 mm ashy grey Larvæ identified by shape of posterior stigmata

Ocular myiasis—In tropical countries larvæ in lids and conjunctival sac Pass into lachrymal passage gain entrance into intraocular tissues Different species *Rhinœstrus bovis Hypoderma bovis Sarcophaga* sp *Gastrophilus intestinalis* and *G equi* also *Œstrus ovis*—bot fly

Eye gnats Family *Chloropidæ* (Hippelates flies) frit flies — Small flies with short aristate antennæ feed on lachrymal secretion sebaceous material pus and blood very persistent convey spirochætes of jaws Larvæ in grass (stem maggots) In California *H flavipes* cause pink eye Eye fly of India Ceylon Java *Siphunculina funicola* is responsible for spread of epidemic conjunctivitis Seasonal prevalence in Assam coincides with appearance of fly

SUBCUTANEOUS MYIASIS

Dermatobia cyaniventris — Macaw worm Ver macaque Œstrid or bot fly S America infests cattle mammals and man Non blood sucking with primitive mouth parts Eggs deposited on leaves in damp places in haunts of mosquito (*Janthinosoma lutzi*) other species and other insects *e g* flesh flies stable-flies (Stomoxys) and some species of tick Packets of eggs in cement softened by moisture adhere to insect thorax and are thus conveyed to man and animals Larva at early stage has swollen head elongated tail = *ver macaque*

female dies and parts slough away Larvæ hatch in soil in 3–4 days pupate on 6th imago emerges 17th day Chigger causes inflammation suppuration pea like elevations secondarily infected by pyogenic cocci or even by tetanus Feet commonly infected sometimes hands soles interdigital spaces roots of nails Usually one or two may be hundreds

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later larger ovoid = *torcel* or *berne* surrounded with transverse row of spines falls to ground pupates Hatches in 2 days then penetrates skin forming aperture which exudes black fæces In man in head arms back abdomen scrotum thigh axilla Pain + when larva is active

Treatment—Remove without incision larva slips out of aperture widened by forceps

Cordylobia anthropophaga—Tumbu fly Ver du cayor Tropical and Central Africa Flesh eating fly 8 5–11 5 mm yellowish grey with brown wings closely resembles *Auchmeromyia* (male *Cordylobia* distinguished by closely set eyes) Usually inactive but rapid flight when disturbed Egg laid in soil white larvæ easily visible search actively for host provided with special mouthparts and cuticular spines to aid penetration of skin of forearm scrotum upper thigh and buttock Lesions resemble inflamed tumour no suppuration Larva emerges in 6–7 days Pupa has square truncated extremity and is found in rat holes Metazoal immunity produced by repeated infection of skin of guinea pigs which eventually become resistant Immune skin grafts on to non immune animal retain and impart immunity

Blood sucking Fly Larvæ (*Auchmeromyia luteola*)— Congo floor maggot Africa N Nigeria to Natal Adult fly 10–12 mm stoutly built orange buff with numerous black hairs Large head separated eyes two dark longitudinal stripes on thorax Second abdominal segment in female twice length of male Smoky brown wings with conspicuous venation Usually sits motionless on thatch beams cobwebs and walls of native huts difficult to see Eggs deposited in cracks and crevices of mud floor especially if contaminated by urine

Congo floor maggot 15 mm is the larva found under sleeping mats in crevices and in moist earth to depth of 3 ft emerges to feed on blood at night drops off when disturbed Dirty white semi transparent with eleven segments at posterior part of each of which are three short limbs and transverse spines which enable larvæ to move rapidly Paired groups of minute teeth form a cupping apparatus on anterior segment Dorsal diverticulum (food reservoir) opens into œsophagus and forms conspicuous red object after feeding on blood Pupa reddish brown oblong 9–10 5 mm by 4–5 mm pupal stage lasts 2–3 weeks

INTESTINAL MYIASIS

Residence in intestinal canal is a feature in life history of diptera Eggs licked from skin or swallowed in food hatch in stomach where larvæ develop and appear in fæces and vomit Ringed cylindrical ½–1 in in length beset with little spines or hairs Over 20 species recognized in human fæces Usually *Fannia canicularis* (small house fly) *F scalaris* *Musca domestica* or *Piophila casei* (cheese maggot) In Africa *Chrysomyia chloropyga* and *C putoria*

Occasionally cause abdominal pain diarrhœa and vomiting

Treatment—Expelled by dose of castor oil

CHAPTER XIII

METAZOAL DISEASES HELMINTHIC INFECTIONS

TREMATODES

FASCIOLIASIS

Fasciola hepatica parasite of liver rot in sheep.—Over 150 cases in man probably quite common Cuba Venezuela Argentine Central Europe Greece England Found in portal vein and subcutaneous abscesses usually causes little disturbance possibly cirrhosis of liver In Syria epileptiform fits associated with buccopharyngeal infection— halzoun

Typical trematode leaf shaped 2–3 cm by 8–13 mm Anterior extremity narrow containing oral sucker ventral sucker larger 3 mm from anterior extremity Branched intestinal cæca with diverticula Egg (found in fæces) operculated 140 μ by 90 μ ovoid brown bile stained Ciliated miracidium develops in eggs 2–3 weeks enters freshwater snails *Limnæa truncatula* (Europe) *L pervia* (Japan) *L viceltrix* (Cuba) becomes sporocyst daughter sporocysts rediæ then cercariæ in 2 months Cercaria blunt tailed settles on grass secretes mucus to form cysts then as metacercaria eaten by host Human infection contracted by eating watercress in meadows frequented by sheep

Treatment—None really effective Emetine injections 10–12 gr in separate courses also big doses of mag sulph with intravenous neostibosan

Fasciolopsis buski normally parasite of pig reservoir for man—China India (Assam) Malaya Sumatra Borneo In Assam 50 per cent infested only small number show symptoms

Resembles *F hepatica* but larger found in small intestine rarely in stomach Flesh coloured elongated oval 3 cm by 12 mm Transverse row of spines numerous near ventral sucker which is larger close to oral Intestinal cæca simple with two characteristic curves towards mid line Egg operculated 130 μ by 80 μ yellow numerous in fæces In water forms in 3 weeks a ciliated miracidium which develops in fresh water snails—*Planorbis cænosus P schmackeri P hemisphærula*—sporocyst in 3 days Rediæ daughter rediæ cercariæ (whole cycle 2 months) Cercaria short lived lophocercous (membranous tailed) well developed digestive tract encysts as *metacercaria* on fresh water plants—water calthrop (ling) *Trapa natans* (China) *T bicornis* (India) also *Spirodela polyrhiza* Metacercariæ adhere to outer skin of ling and are torn off by teeth Plants grown in ponds are fertilized by human fæces therefore *F buski* limited to distribution of plants Cysts taken into mouth pass through stomach excyst in duodenum become attached to intestinal wall

Clinical features—1–2 000 flukes often in small intestine causing alternate diarrhœa and constipation Fæces offensive pale yellow

Œdema of face abdominal wall genitalia and legs sometimes ascites Discomfort may simulate duodenal ulcer Death from exhaustion rare

Treatment —β naphthol gr 10 oil of eucalyptus, min 3 tetrachlorethylene ʒ i hexyl resorcinol, 0 4 gm for child under seven 1 gm from 13 upwards all effective

CLONORCHIASIS

Biliary and hepatic disease caused by *Clonorchis sinensis*

Geographical distribution and epidemiology —Disease of Far East, India Mauritius Japan, Korea, Formosa Indo- and S China Recently new area on Pacific Coast of America and California In fish rais ng provinces in China 50–67 per cent. of native population affected

Ætiology —*Clonorchis sinensis* inhabits biliary passages of man dog cat pig rat mouse badger camel Usually in adult man May invade pancreas and ducts rarely duodenum never gall bladder

Spatulate fluke 10–20 mm by 2 5 mm Cuticle has no spines oral sucker is larger than ventral Intestinal cæca are simple Genital pore in mid line in front of ventral sucker Testes branched in posterior part of body Cross-fertilization as in other members of group Sperms enter female opening of genital pore pass through uterus to spermatheca

Egg 28–30 μ by 15–17 μ operculated contains miracidium and has terminal spine resembling miniature electric light bulb susceptible to desiccation killed by decomposition viable in water 5 weeks ingested by snail before escape of miracidium which has life span of 20 minutes Development in *Bithynia* (*Parafossarulus*) *striatula* (Japan Korea Formosa) *B fuchsiana* and *B longicornis* and *Melania hongkongensis* (China) Miracidium pierces œsophagus casts cilia and becomes sporocyst later elongated rediæ pass into peri œsophageal sinus and move tailwards into liver within 5 weeks Cercariæ two pigmented eye spots blunt tail emerge into water where within 24–48 hours they encyst as metacercariæ in muscles and under scales of freshwater fish *e g* Cyprinidæ Anabantidæ 34 species susceptible Cercarial glands have histolytic secretion dissolving skin Metacercaria secretes viscous fluid forming inner cyst is then encapsulated by fibrous layer in fish then eaten half raw or pickled in *soy sauce*

Adolescercaria —Fully developed cyst protective capsule against gastric juice withstands temperature of 50–70 C for 15 minutes Cyst wall digested by succus entericus in duodenum near papilla of Vater Adolescercariæ escape attach themselves to mucosa and attain maturity in 26 days By chemotaxis a small proportion reach bile ducts Egg production very large—200–400 daily 21 000 flukes may be found at autopsy Life span 12 years

Pathology —*C sinensis* thickens biliary canals passes into cavities and diverticula communicating with bile ducts which contain large number of flukes Liver is enlarged and cirrhotic spleen

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FASCIOLIASIS

Fasciola hepatica parasite of liver rot in sheep —Over 150 cases in man probably quite common Cuba Venezuela Argentine Central Europe Greece England Found in portal vein and subcutaneous abscesses usually causes little disturbance possibly cirrhosis of liver In Syria epileptiform fits associated with buccopharyngeal infection— halzoun

Typical trematode leaf shaped 2–3 cm by 8–13 mm Anterior extremity narrow containing oral sucker ventral sucker larger 3 mm from anterior extremity Branched intestinal cæca with diverticula Egg (found in fæces) operculated 140 μ by 90 μ ovoid brown bile stained Ciliated miracidium develops in eggs 2–3 weeks enters freshwater snails *Limnæa truncatula* (Europe) *L pervia* (Japan) *L viatrix* (Cuba) becomes sporocyst daughter sporocysts rediæ then cercariæ in 2 months Cercaria blunt tailed settles on grass secretes mucus to form cysts then as metacercaria eaten by host Human infection contracted by eating watercress in meadows frequented by sheep

Treatment —None really effective Emetine injections 10–12 gr in separate courses also big doses of mag sulph with intravenous neostibosan

Fasciolopsis buski normally parasite of pig reservoir for man — China India (Assam) Malaya Sumatra Borneo In Assam 50 per cent infested only small number show symptoms

Resembles *F hepatica* but larger found in small intestine rarely in stomach Flesh-coloured elongated oval 3 cm by 12 mm Transverse row of spines numerous near ventral sucker which is *larger close to oral* Intestinal cæca *simple* with two characteristic curves towards mid line Egg operculated 130 μ by 80 μ yellow numerous in fæces In water forms in 3 weeks a ciliated miracidium which develops in fresh water snails—*Planorbis cœnosus P schmackeri P hemisphærula*—sporocyst in 3 days Rediæ daughter rediæ cercariæ (whole cycle 2 months) Cercaria short lived lophocercous (membranous tailed) well developed digestive tract encysts as *metacercaria* on fresh water plants—water calthrop (ling) *Trapa natans* (China) *T bicornis* (India) also *Spirodela polyrhiza* Metacercariæ adhere to outer skin of ling and are torn off by teeth Plants grown in ponds are fertilized by human fæces therefore *F buski* limited to distribution of plants Cysts taken into mouth pass through stomach excyst in duodenum become attached to intestinal wall

Clinical features —1–2 000 flukes often in small intestine causing alternate diarrhœa and constipation Fæces offensive pale yellow

Œdema of face abdominal wall genitalia and legs sometimes ascites Discomfort may simulate duodenal ulcer Death from exhaustion rare

Treatment—β naphthol gr 10 oil of eucalyptus min 3 tetrachlorethylene ʒ 1 hexyl resorcinol 0 4 gm for child under seven 1 gm from 13 upwards all effective

CLONORCHIASIS

Biliary and hepatic disease caused by *Clonorchis sinensis*

Geographical distribution and pidemeiology—Disease of Far East, India Mauritius Japan Korea Formosa Indo- and S China Recently new area on Pacific Coast of America and California In fish raising provinces in China 50–67 per cent of native population affected

Ætiology—*Clonorchis sinensis* inhabits biliary passages of man dog cat pig rat mouse badger camel Usually in adult man May invade pancreas and ducts rarely duodenum never gall bladder

Spatulate fluke 10–20 mm by 2 5 mm Cuticle has no spines oral sucker is larger than ventral Intestinal cæca are simple Genital pore in mid line in front of ventral sucker Testes branched in posterior part of body Cross fertilization as in other members of group Sperms enter female opening of genital pore pass through uterus to spermatheca

Egg 28–30 μ by 15–17 μ operculated contains miracidium and has terminal spine resembling miniature electric light bulb susceptible to desiccation killed by decomposition viable in water 5 weeks ingested by snail before escape of miracidium which has life span of 20 minutes Development in *Bithynia (Parafossarulus) striatula* (Japan Korea Formosa) *B fuschsiana* and *B longicornis* and *Melania hongkongensis* (China) Miracidium pierces œsophagus casts cilia and becomes sporocyst later elongated rediæ pass into peri œsophageal sinus and move tailwards into liver within 3 weeks Cercariæ two pigmented eye spots blunt tail emerge into water where within 24–48 hours they encyst as metacercariæ in muscles and under scales of freshwater fish *e g* Cyprinidæ Anabantidæ 34 species susceptible Cercarial glands have histolytic secretion dissolving skin Metacercaria secretes viscous fluid forming inner cyst is then encapsulated by fibrous layer in fish then eaten half raw or pickled in *soy sauce*

Adolescercaria—Fully developed cyst protective capsule against gastric juice withstands temperature of 50–70 C for 15 minutes Cyst wall digested by succus entericus in duodenum near papilla of Vater Adolescercariæ escape attach themselves to mucosa and attain maturity in 26 days By chemotaxis a small proportion reach bile ducts Egg production very large—200–400 daily 21 000 flukes may be found at autopsy Life span 12 years

Pathology—*C sinensis* thickens biliary canals passes into cavities and diverticula communicating with bile ducts which contain large number of flukes Liver is enlarged and cirrhotic spleen

hypertrophied intestine shows chronic catarrh Sometimes found in pancreas duodenum and stomach causing ascites and anasarca Carcinoma may ensue Death from cirrhosis of liver

Clinical features—Enlargement of liver chronic diarrhœa recurring icterus anasarca cachexia fatal in several years In mild infections epigastric distress and night blindness

Diagnosis—*Obscure hepatic disease from Far East suggests C sinensis* Eggs in fæces Leucocytosis 30 000 eosinophilia 40 per cent Eggs demonstrated in duodenal juice by duodenal sound

Treatment—Unsatisfactory Intravenous Fouadin (trivalent antimony) *1 5–5 c c 10 or more injections Gentian violet* malachite green and Nile blue all lethal to clonorchis but dosage not satisfactorily settled also these dyes have toxic action on man Continuous non surgical drainage of bile by duodenal tube (cocainizing throat to prevent vomiting) gets rid of many clonorchis eggs and toxic matter and is beneficial as temporary measure

OTHER FLUKES OF LESS IMPORTANCE

Opisthorchis felineus—Inhabits liver and bile ducts Common in man in E Prussia Siberia Annam Philippines also in dog cat glutton pig Fluke 8–11 mm by 1 5–2 mm Egg operculate yellow brown 30 μ by 12 μ Intermediary snail *Bithynia leachi* Development as in clonorchis metacercariæ in tench (*Tinca tinca*) and chub (*Idus melanotus*) Behaves in man as clonorchis but is not specially pathogenic 200 or more may be found at autopsy

Heterophyes heterophyes—In small intestine in large numbers common in man in Egypt China Japan al o in fox dog wolf cat

Minute pyriform 1–1 7 mm by 0 3–0 7 mm grey uterus showing as brown patch in centre ventral sucker three times size of oral muscular ring armed with teeth cuticle thickly set with quadrate scales Egg 20–30 μ by 15–17 μ *light brown contains ciliated* miracidium develops in brackish water snails—*Melania tuberculata Cleopatra bulimoides* and in Egypt *Pironella conica* Cercaria with eyes lophocercous Metacercaria in mullet (*Mugil cephalus*) minnow (*Gambusia affinis*) Produce infection when eaten improperly cooked other species recognized *H brevicæca* and *H taihokui* and in Japan *H katsuradai* stouter species

Clinical features and treatment—*Imparts coffee* ground appearance to intestinal wall Enormous numbers adherent to small intestine *May give rise to diarrhœa Eggs found in intestinal* wall and myocardium *Claimed in Manila that it gives rise to symptoms* resembling cardiac beriberi *Readily removed* by thymol 60 gr or oleoresin of aspidium 60 min

Metagonimus yokogawai—Very common in Far East *Korea* Japan Formosa and Balkan States In upper small intestine of man cat dog pelican

Smallest fluke in man 1 1 mm by 0 42–0 7 mm cuticle covered

with small spines ventral sucker displaced to left otherwise resembles above Eggs 33 μ by 21 μ regularly ovoid Develops in *Melania libertina* and *M ebenina* Cercariæ lophocercous anterior end armed Metacercaria encyst under scales of fish—*Plecoglossus altivelis*—eaten raw by Japanese

Clinical features—Probably causes catarrh and diarrhœa

Treatment—As for *H heterophyes*

Echinostoma lindoensis—Philippines and Celebes (Lake Lindoe) Typical echinostome with spines round anterior sucker In large numbers in jejunum causing diarrhœa abdominal pain slight eosinophilia Develops in two intermediary snails *Anisus sarasinorum* and *A contexusculus* metacercariæ in mussels—*Corbicula lindoensis* *C subplanata*

E ilocanum and *E malayanum* in Malaya Natural host pig snail host—*Gyraulus prashadi* *E jassyensis* in Rumania *E recurvatum* in Java and *E surfartyfex* in Assam

Dicrocœlium dendriticum (*D lanceatum*) Normal host sheep found in biliary tract of man Germany Italy France Egypt China Eggs passed in fæces do not hatch in water ingested by land snails—*Zebrina detrita Helicella candidula H itala Torquilla frumentum Cochlicella acita* and others *Pila scorchis javanensis* in intestine of Javanese—together with *E ilocanum*—normal host amphibia and bats develops in snail—*Sta nicola emarginata angulata*

Treatment—Efficacious *Filix mas* min 90 trichlor or tetrachlor ethylene min 40–60

PARAGONIMIASIS LUNG FLUKE

Paragonimus ringeri P westermani and allied species (lung flukes) in lungs of man dog wolf leopard cat mink pig otter ichneumon Produce lung disease associated with hæmoptysis

Geographical distribution and epidemiology—China India Japan Korea Philippines recently also in U S A and West Africa

Ætiology—*P ringeri P westermani* and *P compactus* commonest species in man show minor distinctions 8–20 mm by 5–9 mm oval reddish brown round in section ventral sucker larger and anterior to centre of body Intestinal cæca run zigzag course body bisected by large excretory vesicle Cuticle studded with wedge shaped spines Operculated eggs in sputum 90 μ by 55 μ with thickening at pole opposite operculum

Life history complicated Eggs voided into cystic pockets in lungs escape in sputum and fæces ciliated miracidium hatches in 4–7 weeks and enters snails *Melania tuberculata* (Japan China) *M libertina* (Korea) *M obliquegranulosa* (Formosa) also other species In snail forms sporocyst rediæ and cercariæ (with knob-like tail and anterior stylet) Metacercariæ in various fresh water crabs—*Potamon obtusipes P dehaani P sinensis Sasarma dehaani Eriocheir japonicus Cambaroides similis* (Korea) Metacercariæ in liver muscles and gills of crab eaten raw by man

enters his stomach where the cyst wall is digested *Adolescercaria* emerges traverses abdominal cavity penetrates pleura reaches bronchioles forms cystic cavities and becomes adult which can remain viable in the human body 20 years or longer

Pathology—Small brown spots in lungs scattered burrows towards periphery areas the size of a filbert nut each with 2 or more flukes 13 000 eggs coughed up every day Often associated with T B Also found in liver intestine skin testes muscles and brain (where it forms tunnelled tumours) Eggs in fæces and spinal cord may give rise to transverse myelitis Hundred flukes found in psoas abscess

Clinical features—Insidious onset chronic cough distress in chest Abundant brown pneumonic sputum containing numbers of brown thick shelled operculated eggs irregular hæmoptysis Clubbed fingers lungs show hyper resonance rales and rhonchi Abdominal symptoms dull pains and diarrhœa enlargement of liver appendicitis adenitis *prostatic enlargement and epi* didymitis often Cerebral symptoms especially in children, Jacksonian epilepsy hemiplegia aphasia visual disturbances Cutaneous ulceration sometimes

Diagnosis—Eggs and Charcot Leyden crystals in sputum and fæces T B may co exist Eggs to be differentiated from *Schistosoma japonicum* Blood leucocytosis 15 000 (no eosinophilia) X rays (lipiodol) not conclusive opacities and infiltration sometimes seen Complement fixation test (extract of *Paragonimus* as antigen) sometimes employed

Treatment—Unsatisfactory Emetine intramuscularly 1 gr for 7 days in courses Intramuscular sulphonamides have been favourably reported on Improvement follows lipiodol injections into bronchi

Prophylaxis—Destroy sputum and fæces of infected patients Prohibit sale of crabs which carry parasite Educational methods

SCHISTOSOMIASIS (Bilharziasis)

Groups of diseases widespread in tropics and subtropics Unisexual (sexes separate)—trematodes inhabiting lumen of veins Three species in man (1) *Schistosoma hæmatobium* (2) *S mansoni* (3) *S japonicum*

(1) URINARY SCHISTOSOMIASIS (*Schistosoma hæmatobium*) (*Bilharzia hæmatobia*)

Epidemiology—Great antiquity in Egypt eggs found in mummies *of First Dynasty Widespread in Egypt now* in Delta 60 per cent are infected with *S hæmatobium* and *S mansoni* In Northern Nile Valley Cairo Assiut *S hæmatobium* 50 per cent *S mansoni* absent Heavy infection associated with perennial irrigation with alternate drying and flushing Where 5 per cent population infected 1 1 000 die where 60 per cent 1 22

S hæmatobium—Found in Africa (Cape especially) isolated foci

in Portugal Corsica Cyprus Palestine Arabia Madagascar Reunion Iraq imported in 1901 into Perth W Australia (has now died out) Recent discovery of endemic focus in Bombay State at Gimvi in the Ratnagiri district near the Korkan Coast Species of adult schistosome uncertain Cercariæ found in *Ferrissia tenuis* an ancylid snail

Habitat.—Veins (mesenteric portal vesico prostatic pelvic uterine plexus vesical occasionally vena cava pulmonary) 300 or more found at autopsy in submucosa of bladder *S hæmatobium* long lived (20–37 years) may produce carcinomatous changes Sexes live apart at first when mature female enters gynæcophoric canal of male Experimentally rats mice guinea pigs monkeys hamsters and hedgehogs susceptible

Male—1 5 cm by 1 mm white cylindroid outer surface beset with tuberculations Larger oral and ventral suckers closely situated Ventral infolding of male forms gynæcophoric canal containing female Delicate spines on suckers Four to five testes posterior and dorsal to ventral sucker Progresses along veins carrying female

Female—2 cm by 0 25 mm darker in colour filiform middle portion in gynæcophoric canal anterior free Body smooth papillæ on posterior end Ovary and yolk glands anterior to intestinal cæca genital pore median posterior to ventral sucker anterior part of uterus contains terminal spined eggs Genital openings of both sexes face each other In both sexes alimentary canal commences at prehensile oral sucker œsophagus with two dilatations bifurcates in front of ventral sucker to form intestinal cæca uniting again into median trunk

Egg—Oval, 150 μ by 60 μ short stout terminal spine contains ciliated *miracidium* head towards blunt end active so it can turn about Egg shell permeable to antimony salts Eggs of *S hæmatobium* often in fæces especially in Upper Egypt and Congo (see also *S intercalatum*) Also in lungs brain spinal cord

Miracidium—In contact with water shell *enlarges becomes softened* by lytic ferment and bursts by transverse rupture liberating miracidium Egg remains alive in sterile urine or moist fæces 2–3 weeks Miracidium remains active in water for 24 hours has anterior papillary beak swims by cilia and muscular action Has primitive alimentary canal two cephalic salivary glands excretory tubules and flame cells

Process of escape of eggs from tissues—Paired worms travel to narrowest point Female leaves male penetrates into venules deposits eggs and retracts so that spine of egg engages vein walls and escapes into tissues Others think that spine facilitates adherence of ova to vessel wall The ovum plays a passive part but endothelial lining is the active factor only ova laid in blood vessels close to the bladder pass to outside whilst others are held in the tissues

Development (on general lines applicable to all three species)—Miracidia penetrate air sac and tentacles of snail of genus *Bulinus*

(several species) papilla bores in If heavily infected snail dies Cilia cast penetrates liver (hermaphrodite or digestive gland) *via* lymph spaces Infection only in warm season (Egypt) Liver of snail turgid swollen yellow or orange infected individual snails can thus be recognized Elongated thin walled sporocyst produces daughter sporocysts which *penetrate gland* Developmental cycle occupies 6 weeks under optimal conditions a single miracidium produces 100 000–250 000 cercariæ

Schistosome cercariæ —Bifid tailed cercariæ formed within sporocysts then escape Diurnal discharge from pulmonary cavity of snail Cast off tail on entering skin of host (man) Penetration aided by acid secretion of glands Most die in transit Three hundred may *enter mouse and only 20 adults develop Cercariæ adhere to body* of host by ventral sucker therefore penetrate mucous membrane mouth or œsophagus women and children in Egypt infected by drinking as well as by Mohammedan ceremonial of cleansing mouth with water In bathing movement of water attracts cercariæ to skin Entry causes dermatitis

Body elongated forked tail 0 48 mm Head and tail approximately *equal length Cuticle with spines anterior (oral) median* muscular ventral sucker anterior sucker larger than ventral Central part occupied by circumoral glands—conspicuous peri acetabular opening by ducts on rectractile papillæ surrounding mouth which is small oval and anterior Five peri acetabular glands with conspicuous nuclei acidophil *Cercariæ phototactic emerging from* snail 9 a m to 2 p m no emergence on dark days 50–1 000 daily optimum temperature 32–33° C (89 6–91 4 F) (for *S mansoni* 15–35° C 59–95° F) Abundant oxygen necessary cannot feed swims with ease in water circular movement propelling towards tail Rests with tail prongs on surface slowly *sinks absorbs* oxygen through tail then rises again Life span 48 hours *most active for 24* more so when water disturbed Warmth is chief factor in attraction to host Infection by cercariæ easy in laboratory insert tail of mouse in water containing cercariæ

On entry loses cephalic glands becomes *schistosomulum* and adult in portal vein in 6 weeks travels *via* bloodstream veins heart lungs some through pulmonary *capillaries some even to skin* causing secondary skin reactions *e g* urticaria When mature pairs in portal vein goes back against stream to mesenteric veins eggs are carried back and deposited in liver and spleen Discharge of digestive products causes fibrosis and black pigment from digested r b c pigment *like that of malaria*

No general agreement on differential details of structure in cercariæ *of the three human species average 0 4–0 5* mm probably individual differences in different batches on the whole cercaria of *S japonicum* is smaller All have 5 pairs of salivary mucin periacetabular glands (This account is applicable *to other* human cercariæ)

N B —Innumerable trematode cercariæ in freshwater snails in

tropics Life history of many unknown All schistosome cercariæ of man mammals and birds have forked tails

Cercarial dermatitis produced by entrance of cercariæ into skin (in human schistosomiasis) also by penetration of other species—*e g* swimmers itch —emerging from *Limnæa* the common pond snail. *Cercaria elvæ* in Lake Michigan *C ocellata* in Lake Roath S Wales (probably Bilharziella of water birds) In Malaya and India blotchy papular rash with central punctures produced by cercariæ of *S spindale* of water buffalo

Intermediary molluscan hosts —*Bulinus contortus* *B dybowski* (Egypt) *B innesi* (Sudan) *B truncatus* (Palestine) *B* (*Pyrgophysa*) *forskali* (Mauritius N Nigeria Kenya) *B globosus* (Sierra Leone Nyasaland) *B africanus* (Natal) *Isodora ovoidea* (Zanzibar) *Physopsis nasuta* (Kenya) (Exception *Planorbis* (*Biomphalaria*) *dufouri* Portugal and Morocco *Melania nodocincta M tuberculata* Nyasaland)

Development in snails vicarious *B forskali* cannot be infected in the Belgian Congo but is the chief vector in N Nigeria

Genus Bulinus spiral snails non operculate opening sinistral body contains red hæmoglobin pigment (Some conchologists recognize three species—*contortus dybowski innesi*—as subvarieties of *B truncatus*)

S INTERCALATUM (*Bilharzia intercalata*)

Variety from Upper Congo, close to *S hæmatobium* but resembles *S bovis* differentiated by egg found only in fæces *Egg* 140–240 μ by 58 85 μ, spine long r 20 μ spindle shaped resemble those of *S matthei* or *S bovis* great variation in shape and size Spinster females often in small numbers. Intermediary snails *Bulinus africanus* *B globosus*

Pathology —At first injection of mucosal vessels of urinary bladder then papules eggs in blood vessels trigone usually first affected granular phosphatic deposit (sandy patches) clusters of eggs principally in submucosa some calcified Polypoid excrescences adeno papillomata frequently contain adult schistosomes Nodules of subperitoneal surface may resemble T B Muscular coats of bladder hypertrophied capacity diminished mucosa covered with blood stained mucus + eggs in large numbers Then phosphatic gravel or stones appear in lacunæ in bladder wall or free in cavity

Usually lower end of ureter is affected and sometimes renal pelvis secondary *hydronephrosis* common (important) Blockage of ureter with calculi common Hyperplasia of prostate due to egg Secondary ascending infection of urinary tract—pyelitis renal abscess etc —and vesiculæ seminales vaginal wall cervix hypertrophy of glans penis with urethral blockage Eggs demonstrated by digesting tissues in 3 per cent potash solution Found in small numbers in liver gallstones heart kidneys lungs brain spinal cord sometimes form tumours of peritoneum and uterine ligaments

Clinical features —Symptoms vary great majority mild Hæmaturia almost invariable Egyptian peasants regard it as a sign of

puberty In hyperinfection urinary sepsis and death Incubation period of disease 3 *months to* 2½ years 3 periods 1 Invasion 2 Deposition 3 Terminal

Period of invasion —Cercarial dermatitis on infection blotchy papular rash severe itching

Invasion stage —Pyrexia urticaria abdominal pain high eosinophilia (*see* p 200)

Deposition stage —Polyuria aggravated by exercise with terminal hæmaturia Blood clots *sometimes containing eggs deposited on* standing in conical glass Dull *sense of suprapubic oppression* deep seated perineal pain scalding on micturition Cystitis with pain often septic Sometimes adult worms passed in urine Frequency often rectal pain sometimes with blood and mucus containing *S hæmatobium* eggs (or double infection with *S mansoni*) Lasts for months or years Spontaneous recovery rare

Terminal stage —Eggs form nuclei for phosphatic calculi symptoms of vesical or ureteric calculus dilatation *of ureters with hydro*nephrosis superimposed carcinomatous changes may cause exacerbation of symptoms Hypertrophic contraction or dilatation of bladder hæmaturia + Involvement of prostate and vesiculæ seminales spermatorrhœa secondary infections (streptococcal) common Anæmia hectic fever debility death *Urinary fistulæ* on perineum or posterior surface scrotum caused by infiltration of eggs In urethra stricture results Schistosomiasis of spermatic cord and epididymis (tunica and testes seldom) Cord nodular bilharzial rosary Primary schistosome disease of gall bladder rare Sometimes bilharzial appendicitis in N Nigeria 57 per *cent of appendix cases in natives are bilharzial* Vaginitis and cervicitis papillary growths and ulcers like carcinomata *papillomata* in vagina round anus and perineum to be distinguished from venereal warts Eggs in lungs cause interstitial pneumonia and arterial changes resembling Ayerza s disease in brain and spinal cord cause epileptic attacks occasionally transverse myelitis

Diagnosis —Eggs in urine especially terminal portion demonstrated by deposition in urine glass or centrifugation When scanty diagnosis is difficult character of deposit mucus + phosphatic crystals pus cells bladder epithelium eosinophiles usually ++

Cystoscopy —Examine shreds of mucus for eggs Appearances of mucous membrane of bladder especially in trigone sparse grey discrete elevations round ureteric orifice later hæmorrhagic areas with surrounding hyperæmia In advanced cases ridges like sea sand together with papillomata

Complement fixation reactions —Performed as for W R Antigen prepared from liver of snails (*Biomphalaria*) infected with *S mansoni* cercariæ Group reaction equally effective with *S hæmatobium S spindale* and *Fasciola hepatica Best results* in early infections before deposition of ova less specific in later cases

(Antigen prepared by macerating infected snail livers in absolute alcohol filtered and evaporated by Sprengel s pump saline extract made)

Intradermal test —Similar to Casoni reaction (*see* p 240) A saline extract (*vide* above) of livers of *Pl exustus* infected with *S spindale* filtered made bacteria free and injected intradermally (4 minims) Positive reaction immediate wheal zone of erythema with outrunners Delayed reaction 5–18 hours Diagnostic for schistosome group persists for years after cure

Differential diagnosis —From vesical calculus T B cystitis renal calculus all other forms of hæmaturia filarial hæmatochyluria gonorrhœal cystitis prostatic disease

Treatment —Intravenous injections of sodium antimony tartrate (Tartar emetic) Schistosome adult affected by antimony especially ovary cercariæ and miracidia less so Prevents hatching of eggs in water eggs become dark and shrivelled after 10 gr of antimony tartrate

1 *Sodium-antimony tartrate* intravenous injection alternate days for 4–6 weeks commencing with ½ gr in 10 c c of distilled water increase by ½ gr to maximum (for adults) 2½ gr Total dosage 25–30 gr Toxic phenomena avoided by addition of 5 per cent glucose Rapid improvement eggs and blood disappear after 15 gr For children under 10 dose of 0 1 gr is sufficient maximum 1 gr If course is interrupted must be recommenced *ab initio* Toxic effects coughing retching vomiting flushing More severe antimony reaction headache arthritic pains in shoulder joints *Pentavalent compounds of antimony not effective*

2 *Fouadin* (13 per cent trivalent antimony compound—antimony pyrocatechin-disulphonate of soda) Used in Egypt cure in 19 days in over 90 per cent (1930) more rapid than (1) Preferably intramuscularly into buttock or intravenously in 7 per cent solution dosage 1 5–5 c c one dose of 1 5 c c one 3 5 c c 7 of 5 c c total of 9 injections maximum 15 Average quantity of antimony 0 4 gm excreted in urine and fæces Late vomiting sometimes No severe local reaction at site of injection Sometimes toxic necrosis of liver follows with death Intravenous injections satisfactory on alternate days Used in S Africa for children

3 *Anthiomaline* (antimony thiomalate of lithium) now considered better than tartar emetic (in ampoules 6 per cent solution 10 per cent antimony) Total necessary 50 c c (or 0 3 gm metallic antimony) Intravenous 0 5 c c for children 1 5 c c for adults maximum 4 c c Intramuscularly 12 injections on alternate days (one of 1 5 c c one of 3 and 10 of 4 25 c c total 47 c c) Living ova not passed after 21 5 c c *Local reaction (pain) sometimes* general reaction negligible

4 *Emetine hydrochloride* Toxic to schistosomes Given intravenously but not recommended on account of toxic action useful

for those resistant to antimony ½ gr in solution maximum for child 1 gr total 15 gr Adults 1½ gr daily total 20 gr Intra muscularly less effective

5 *Miracil D* (hydrochloride of 1 methyl 4 beta diethyl aminoethyl aminothioxanthone or *lucanthone*) in tablets each of 0 5 gm Total dosage 60 mg per kg divided into 6 doses (2 daily for 6 days) Children 6–10 one tablet morning and evening first day same on second ½ tablet morning and evening on the third Total 2 5 gm 10–14 total dosage 3 gm For adults 1½ tablets first morning followed by 1 tablet the same evening on each of two subsequent days Total dosage 3 25 gm For heavy adult (180 lbs) total dosage 5 5 gm 2 tablets morning and evening each of the two first days and on the third morning and one tablet on the third evening Drug cures 60 per cent infected with *S hæmatobium* Less effective for other types Overdose produces insomnia and yellow skin discolouration Miracil D must be kept at high blood level

)cal treatment—Calculi removed by operation Perineal cystotomy and drainage Treat perineal fistulæ and hyperplasia of cervix and vagina by scraping

·ognosis—Greater exposure to infection means more severe clinical cases If treated early prognosis now very good as calculi and secondary infections are avoided In mild cases with occasional hæmaturia there is no serious injury to health and usually spontaneous cure Re infection must be avoided At present all natural sources of infection in Africa and Palestine are known

rophylaxis (refers also to *S mansoni*)—Complicated and difficult in heavily infected countries like Egypt Educational methods (posters films) necessary Children especially warned by school and religious teachers against paddling bathing and washing in rivers ponds and canals Clearness of water no criterion Brackish water safe Sportsmen shooting duck or snipe should wear gum boots Drinking boiled water is safe but chlorinated water is not lethal to cercariæ Every care must be taken to avoid soiling water supplies by urine or excreta Measures against molluscs and ova (spawn) molluscs widely disseminated by water birds *Bulinus* soon appears in temporary collections of water in Western Desert many miles away from Nile Periodic drying of canals temporarily effective Canals now treated in Egypt in non irrigation season—April to July—when they contain less than half normal volume of water by calculated amount of *sizolin* (creosote derivative) 1 20 000 which destroys snails and cercariæ Difficult to get permanent results owing to opening of sluice gates in spring and restocking of snails from Nile Organization of antischistosome units in Egypt combines prophylaxis with mass treatment of infected population Results so far favourable but necessarily slow Molluscicides now applied to stagnant canals and drains—Sodium pentachlorate and dinitro-o-cyclo hexylphenol (DCHP) at 5 and 10 parts per million respectively

(2) INTESTINAL SCHISTOSOMIASIS (*Schistosoma mansoni*) (*Bilharzia mansoni*)

Chronic endemic disease with dysenteric and abdominal symptoms and sometimes with splenomegaly Common in Egypt Central Africa Nyasaland

Geographical distribution and epidemiology—Probably originally an African disease imported into W Indies and S America by slaves At present in Africa generally Egypt Congo W Africa E Africa (Abyssinia Eritrea Zanzibar Rhodesia Tanganyika Kenya Madagascar Natal Transvaal) S America Brazil Venezuela Guianas W Indies (especially Antigua) In St Kitts in imported African green monkey (*Cercopithecus sabæus*) In Lake Tanganyika natural infection of house rats found In Central Africa experimental infection of *Mastomys coucha* the pouched rat

Usually more common in men In Sierra Leone in adult women Range of *Schistosoma mansoni* limited by that of intermediate molluscan host closely associated with *S hæmatobium* Areas in S Egypt, S Sudan and W Africa where *S mansoni* only is found Infection acquired during period of shallow water to permit high concentration of cercariæ In inland lakes October to January in backwaters of Nile February–June

Ætiology—*S mansoni* very similar to but smaller than *S hæmatobium*

Male 1–1 2 mm by 1 mm ventral sucker and wart like tuberculations more pronounced *Intestinal canal bifurcates at ventral sucker* Intestinal cæca unite anteriorly to form single long intestinal tract 8–9 small testes

Female 1 2–1 6 cm as in male intestinal cæca unite in anterior half Ovary situated in anterior half in front of union of intestinal cæca Uterus short usually with few lateral spined eggs Shape of bulb of shell-gland determines shape and position of spine

Habitat—Inferior and superior mesenteric veins hæmorrhoidal plexus portal system Eggs deposited in subterminal branches of mesenteric veins escape aided by lateral spine In intestine some pass through muscularis mucosæ *via* capillaries when in numbers produce dysenteric symptoms Eggs 150 μ by 60 μ lateral spine 20 μ considerable variation Miracidium similar to that of *S hæmatobium* may be larger if fæces liquid miracidia escape into lumen of bowel

Life history—Development in molluscan host identical with that of *S hæmatobium* eggs escape mostly in fæces small proportion in urine Development mostly in snail genus *Planorbis* (*Biomphalaria*)—flat whorled ammon horned snails like *P corneus* common pond snail in England—*Planorbis boissyi* (Egypt) *P alexandrinus* and *P herbeni* (Sudan) *P neosudanicus* (Nyasa land) *P pfeifferi* (Sierra Leone S Africa Rhodesia) *P philippici sub angulatus* (Tunis) *P gibbonsi* (Zanzibar) *P stanleyi* (C

for those resistant to antimony ½ gr in solution maximum for child 1 gr total 15 gr Adults 1½ gr daily total 20 gr Intramuscularly less effective

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Local treatment.—Calculi removed by operation Perineal cystotomy and drainage Treat perineal fistulæ and hyperplasia of cervix and vagina, by scraping

Prognosis.—Greater exposure to infection means more severe clinical cases If treated early prognosis now very good as calculi and secondary infections are avoided In mild cases with occasional hæmaturia there is no serious injury to health and usually spontaneous cure Re-infection must be avoided At present all natural sources of infection in Africa and Palestine are known

Prophylaxis (refers also to *S mansoni*) —Complicated and difficult in heavily infected countries like Egypt Educational methods (posters films) necessary Children especially warned by school and religious teachers against paddling bathing and washing in rivers ponds and canals. Clearness of water no criterion Brackish water safe Sportsmen shooting duck or snipe should wear gum boots Drinking boiled water is safe but chlorinated water is not lethal to cercariæ Every care must be taken to avoid soiling water supplies by urine or excreta. Measures against molluscs and ova (spawn) molluscs widely disseminated by water birds *Bulinus* soon appears in temporary collections of water in Western Desert, many miles away from Nile Periodic drying of canals temporarily effective Canals now treated in Egypt in non irrigation season—April to July—when they contain less than half normal volume of water by calculated amount of *sirolin* (creosote derivative) 1 20 000 which destroys snails and cercariæ Difficult to get permanent results owing to opening of sluice gates in spring and restocking of snails from Nile Organization of antischistosome units in Egypt combines prophylaxis with mass treatment of infected population Results so far favourable but necessarily slow Molluscicides now applied to stagnant canals and drains—Sodium pentachlorate and dinitro-o-cyclohexylphenol (DCHP) at 5 and 10 parts per million respectively

(2) INTESTINAL SCHISTOSOMIASIS (*Schistosoma mansoni*)
(*Bilharzia mansoni*)

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Ætiology—*S mansoni* very similar to but smaller than *S hæmatobium*

Male 1–1·2 mm by 1 mm ventral sucker and wart like tuberculations more pronounced *Intestinal canal bifurcates at ventral sucker* Intestinal cæca unite anteriorly to form single long intestinal tract 8–9 small testes

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(*Bilharziasis mansoni*)

Chronic endemic disease with dysenteric and abdominal symptoms and sometimes with splenomegaly. Common in Egypt, Central Africa, Nyasaland.

Geographical distribution and epidemiology.—Probably originally an African disease imported into W. Indies and S. America by slaves. At present in Africa generally, Egypt, Congo, W. Africa, E. Africa (Abyssinia, Eritrea, Zanzibar, Rhodesia, Tanganyika, Kenya, Madagascar, Natal, Transvaal), S. America, Brazil, Venezuela, Guianas, W. Indies (especially Antigua). In St. Kitts in imported African green monkey (*Cercopithecus sabaeus*). In Lake Tanganyika natural infection of house rats found. In Central Africa experimental infection of *Mastomys coucha*, the pouched rat.

Usually more common in men. In Sierra Leone in adult women. Range of *Schistosoma mansoni* limited by that of intermediate molluscan host, closely associated with *S. hæmatobium*. Areas in S. Egypt, S. Sudan and W. Africa where *S. mansoni* only is found. Infection acquired during period of shallow water to permit high concentration of cercariæ. In inland lakes October to January, in backwaters of Nile February–June.

Ætiology.—*S. mansoni* very similar to but smaller than *S. hæmatobium*.

Male. 1–1.2 mm. by 1 mm.; ventral sucker and wart-like tuberculations more pronounced. *Intestinal canal bifurcates at ventral sucker*. Intestinal cæca unite anteriorly to form single long intestinal tract. 8–9 small testes.

Female. 1.2–1.6 cm.; as in male, intestinal cæca unite in anterior half. Ovary situated in anterior half in front of union of intestinal cæca. Uterus short, usually with few lateral spined eggs. Shape of bulb of shell gland determines shape and position of spine.

Habitat.—Inferior and superior mesenteric veins, hæmorrhoidal plexus, portal system. Eggs deposited in subterminal branches of mesenteric veins; escape aided by lateral spine. In intestine some pass through muscularis mucosæ via capillaries; when in numbers produce dysenteric symptoms. Eggs 150 μ by 60 μ, lateral spine 20 μ; considerable variation. Miracidium similar to that of *S. hæmatobium*, may be larger; if fæces liquid, miracidia escape into lumen of bowel.

Life history.—Development in molluscan host identical with that of *S. hæmatobium*; eggs escape mostly in fæces, small proportion in urine. Development mostly in snail genus *Planorbis* (*Biomphalaria*)—flat whorled ammon-horned snails like *P. corneus*, common pond snail in England—*Planorbis boissyi* (Egypt), *P. alexandrinus* and *P. herberti* (Sudan), *P. neosudanicus* (Nyasaland), *P. pfeifferi* (Sierra Leone, S. Africa, Rhodesia), *P. philippianus*, *sub-angulatus* (Tunis), *P. gibbonsi* (Zanzibar), *P. stanleyi* (C

Kenya) *P adouensis* (Abyssinia) *P cultratus* (Venezuela) (*P*) *Australorbis glabratus* (N Brazil Antigua Venezuela) *A olivaceus* (Brazil and Dutch Guiana) *A centimetralis* (Brazil) *A glabratus* *A antiguensis* (Antilles) *Biomphalaria* new name for *Planorbis* Races of *S mansoni* recognized *Miracidia* from strains of N African race will not develop in appropriate snails from New World

Pathology —*S mansoni* causes grave changes in viscera The eggs in numbers in liver cause pipe stem cirrhosis In mucosa of intestinal canal the characteristic sandy patches are due to effete calcified eggs Deposition of hæmatin pigment in granules in liver (Kupffer cells) Portal and retroperitoneal lymph glands enlarged Usually hypertrophy of spleen (Egyptian spleno megaly) Lesions in colon (1) thickening of mucosa (2) papillomata (3) pericolic tumours (4) polypi which may extrude from anus or (in cæcum) cause intussusception Small intestine rarely affected sometimes lower ileum In colon septic foci and ulceration of bowel caused by tearing off of pedun culated papillomata Ulcers formed (may be superinfected with *Entamœba histolytica*) sometimes perforation Small pericolic nodules and lesions in mesenteric glands may resemble tuberculosis Pulmonary lesions often embolism by masses of eggs filtered out by arterioles producing *arterial* changes resembling Ayerza s disease In 10 per cent adult flukes found in pul monary arteries

Clinical features

1 *Stage of invasion* —Cercarial dermatitis six weeks later toxic manifestations as in Katayama disease (*see* p 204) remittent and intermittent pyrexia urticaria abdominal pain rigors pulmonary symptoms cough hepatic and splenic tenderness localized deep pain over cæcum Pronounced leucocytosis (30–50 000) with high eosinophilia (30–76 per cent)

2 *Stage of deposition* —Localizing symptoms diarrhœa dysentery (blood and mucus with lateral spined eggs) tenesmus sometimes choleraic diarrhœa

3 *Terminal stage* —Massive abdominal tumours (resembling car cinoma) intestinal stasis and prolapse of hypertrophied papillo mata through anus Infiltration of buttocks with eggs fistulæ and induration Cirrhosis of liver with ascites Pneumonia from deposition of eggs in lungs Bilharzial appendicitis massive infiltration of hypertrophied organ In 50 per cent in Egypt double infection with *S hæmatobium* and (almost invariably) with *Ancylostoma duodenale*

VISCERAL SCHISTOSOMIASIS (Egyptian splenomegaly)

Hepatolienal fibrosis with hepatic cirrhosis and splenomegaly in upper and lower Egypt and in N Nyasaland 20 per cent of children under 4 have splenomegaly with profound anæmia Formerly thought separate (Banti s) disease In young severe course with rickets in adults cirrhosis with ascites often complicated by ancylostomiasis

Spleen very large perisplenitis Splenic hyperplasia not caused deposit of eggs but secondary to hepatic cirrhosis Severe anæmia of of secondary type with advanced blood changes eosinophilia marked at first leucocytosis (17 000) with myelocytes then leucope No intestinal symptoms sometimes no eggs of *S mansoni* in fæces demonstrable in liver spleen and other organs by digestion v potash Some consider it due to infection with spinster fema or bachelor males but this is most unlikely Irregular pyre vomiting diarrhœa œdema often purpura hæmatemesis frequ Thrombosis of portal vein sometimes hepatic carcinoma Ven bum heard by stethoscope over liver Course of disease may be p tracted Death from hepatic cirrhosis or pulmonary complication

Pathology —Spleen average weight 30–300 oz (933–9 330 gm contains a few eggs of *S mansoni* and shows hyperplasia v macrophage cells Number of eggs in liver small compared w extensive cirrhosis Multilobular with isolated necrotic f In advanced stages shrinkage of liver

Diagnosis —Lateral spined eggs in fæces—often scanty concentra methods necessary (Fæces shaken up with dilute HCl 1 pa ether 2 parts strained through gauze filtrate centrifug When fæces are shaken up with water eggs hatch and miraci are easily seen Sigmoidoscopy scraping intestinal mucosa biopsy of papillomata or ulcers Rectal swab method much u On rectal examination papillomatous growths may be felt 5 per cent eggs are found in urine In hepatolienal form incre of euglobulin in serum positive formaldehyde test (*see* p 27 not reliable in differentiating leishmaniasis Complement fixat and intradermal test as in *S hæmatobium* Papillomata granulomata cause localized thickening of colon

Papillo-adenomata in rectum to be differentiated from piles carcinoma Egyptian splenomegaly from kala azar Ban disease splenic anæmia and other forms of splenomegaly

Treatment —Gross changes in organs and deposition of fibrous tis more extensive than in *S hæmatobium* infections liver especi involved therefore effects of antimony treatment not so striki Though adult flukes are killed off no striking change may observed in patient Operative measures may be necessary remove adeno-papillomata obstructing lumen of colon

N B —*Pentavalent compounds of antimony not effective*

1 *Tartar emetic* —In early stages as effective as in *S hæmatobi* in same amounts In Surinam early cases in young adults gi on alternate days 3 c c 5 c c 7 5 c c of 1 per cent solutio total 150–200 c c (1½–2 gm) whole course 6–7 weeks So cases require much bigger total dosage up to 60 gr (4 gm) children in Egypt rectal injections of 1 per cent tartar em solution daily for 5–7 days are said to be effective

2 *Fouadin* —Intramuscularly as for *S hæmatobium* (see p 19 not so effective Several courses required After 13 injectio signs of drug intolerance appear and may cause death especi

Kenya) *P adowensis* (Abyssinia) *P cultratus* (Venezuela) (P) *Australorbis glabratus* (N Brazil Antigua Venezuela) *A olivaceus* (Brazil and Dutch Guiana) *A centimetralis* (Brazil) *A glabratus* *A antiguensis* (Antilles) *Biomphalaria* new name for *Planorbis* Races of *S mansoni* recognized *Miracidia from strains of N* African race will not develop in appropriate snails from New World

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in double infections with *S hæmatobium* If there are renal complications fouadin is contra indicated (Urine gives positive catechol test in fouadin therapy green with ferric chloride violet on adding sodi bicarb)

3 *Anthiomaline*—Intravenously results better than with tartar emetic (p 197)

4 *Emetine*—Efficacious but toxic Ten injections total 9 2 gr (0 6 gm) Initial two doses of ½ gr remaining eight of 1 gr

5 *Miracil D* has been tried in Egypt Brazil and elsewhere not so effective as in *S hæmatobium* (p 198)

6 *Operative measures*—Excision of 12–15 inches of rectal and lower sigmoid mucosa (sleeve operation) unsuitable for anæmic or debilitated subjects

7 *Operative measures for Egyptian splenomegaly*—Talma Morrison omentopexy Splenectomy in early cases successful mortality 15 per cent Ascites pellagra cardiac and renal disease are contra indications Preliminary treatment with carbon tetra chlorethylene for ancylostomiasis Neosalvarsan for syphilis *Effects of splenectomy permanent ascites does not develop*

Prognosis—As for *S hæmatobium* Infections often contracted in clear running water

(3) EASTERN SCHISTOSOMIASIS

Schistosoma japonicum (*Bilharzia japonica*) Katayama disease (Japan)

Serious chronic endemic disease of Far East Invasion symptoms severe generalized infections common *Infects domestic animals as well as man*

Geographical distribution and epidemiology—*Mostly in Chinese and* Japanese sometimes in Europeans Local dogs cats horses and imported cattle naturally infected Native cows immune Infection widespread after floods and inundations China (Yangtse in lower reaches) Hunan Hupeh Anhwei Kiangsu and Kiangsi Near Canton and Foochow On Burmese border Yunan N Shan States Japan (Hiroshima and Katayama) S Formosa Philippines—Samar Leyte Mindanao Celebes

Ætiology—*Schistosoma japonicum* differs in important respects from *S hæmatobium* and *S mansoni* smaller non tuberculated easily transmitted to monkeys rabbits mice rats and guinea pigs In Formosa race of non human *S japonicum in domestic animals especially pigs*

Male—9–12 mm *by 0 5 mm Cuticle and mouth no tuberculations* or spines 6–8 testes dorsal to ventral sucker Vasa efferentia *form* common ducts opening posterior to it in large seminal vesicle Posterior portion widens overlapping more extensively than in other species

Female—1 2–1 6 cm by 3 mm (great variation in size) ovary central intestinal cæca unite immediately behind it Well developed yolk glands extending to posterior extremity Uterus

in cortex Schistosomulæ in lungs some may reach liver by traversing mediastinum and diaphragm

Clinical features —Course usually much graver and more rapid than *S mansoni* Massive infections common in some districts but symptomless cases occur with milder degrees

Stage of invasion —Cercarial dermatitis ++ initial fever very severe (Katayama disease) urticaria abdominal pain paroxysmal cough dermatographia Leucocytosis eosinophilia 60 per cent or more

Stage of deposition —Great emaciation dysenteric symptoms enlargement of liver and spleen

Terminal stage —3–5 years hepato lienal fibrosis ascites œdema of legs great anæmia dysenteric symptoms Jacksonian epilepsy hemiplegia blindness (visual centres) eggs in brain Mortality considerable death from exhaustion cholæmia or superadded infections

Diagnosis —*Urticaria with eosinophilia suggestive* Eggs usually numerous in fæces Formaldehyde serum test usually + Com plement fixation and intradermal test positive as in other forms Biopsy of liver (with liver puncture wide bore needle) or opera tion for splenectomy demonstrates eggs

Splenomegaly to be differentiated from splenic anæmia Jacksonian fits from cerebral tumours cysticercosis etc

Treatment —*In early stages tartar emetic 24–30 gr (1 5–1 9 gm)* Most efficacious drug also cures schistosomæ Jacksonian *epilepsy in Europeans Fouadin in similar doses (see p 197)* widely employed in China but most cases are in terminal stages *before seeking treatment* Splenectomy not usually successful on account of advanced cirrhosis of liver Emetine also used (see p 197) but verminous thrombosis of portal vein may ensue Miracil D useless

Prophylaxis —Drying up ditches is no good *Oncomelania* being oper culated Lime (1 per cent solution) used Application of steam jet to mud to destroy snails 1 200 000 copper *sulphate solution* used whenever possible Rubber waders to be worn by sportsmen Education much *less* valuable as *domestic animals* especially dogs infected Snail vectors live in inaccessible places Sodium pentachlorophenate (*santobrite*) applied to soil 390 mg per sq foot twice yearly to ditches banks and rodent burrows At this *concentration* harmless to man and domestic animals Results encouraging 10 pts per million cyclohexyl dinitrophenol said to be better

OTHER TREMATODES

Gastrodiscoides hominis

Geographical distribution —Malaya Assam India Burma Cochin China British Guiana Normal host pig mouse-deer

Ætiology—*G hominis* reddish from hæmoglobin When alive expansive—elongates to 1 cm and shrinks to 5–7 mm by 3–4 mm Anterior sucker conical posterior discoidal flattened ventrally to concave disc prominent genital papilla 2 5 mm from oral sucker Ventral sucker large (2 mm in diameter) Cuticle smooth Pharynx with two pear shaped pharyngeal pouches two lobulated testes ovary in midline posterior to testes *Eggs* 152 μ by 60 μ operculated Life history unknown

Habitat—In cæcum in large numbers induces no symptoms eggs in fæces

Treatment—Thymol and tetrachlorethylene effective

Pseudodiscus (*Watsonius*) *watsoni* once found in negro in S W Africa Normal host monkeys *Cercopithecus* and *Papio*

CHAPTER XIV

METAZOAL DISEASES NEMATODE INFECTIONS

ASCARIASIS

Infection of alimentary tract mostly small intestine of gorilla and large apes and man with roundworm *Ascaris lumbricoides* *A suis* in pig indistinguishable

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

World wide especially in tropics in China India and Pacific Islands A disease of insanitation

ÆTIOLOGY

A lumbricoides—Large like earthworm Round tapering at both ends Mouth anterior guarded by thin lips with finely denticulated margins anus subterminal

Female—20–35 cm by 3–6 mm paired genital tubes containing uterus receptaculum seminis oviduct and ovary tubes and ducts attain length of 125 cm Total capacity 27 million eggs average daily output 200 000 2 400 eggs by one female for each gm of fæces

Male—15–31 cm by 2–4 mm yellow or brown with white longitudinal lines tail curved in semicircle two rows of tactile papillæ and two chitinous spicules

Egg—50–70 μ by 40–50 μ elliptical encased in albuminous coat with mamillated appearance stained brown by fæcal pigments

in cortex Schistosomulæ in lungs some may reach li traversing mediastinum and diaphragm

Clinical features—Course usually much graver and more rapi *S mansoni* Massive infections common in some district symptomless cases occur with milder degrees

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Treatment.—Thymol and tetrachlorethylene effective

Pseudodiscus (*Watsonius*) *watsoni* once found in negro in S W Africa Normal host monkeys *Cercopithecus* and *Papio*

CHAPTER XIV

METAZOAL DISEASES NEMATODE INFECTIONS

ASCARIASIS

Infection of alimentary tract mostly small intestine of gorilla and large apes and man with roundworm *Ascaris lumbricoides* *A suis* in pig indistinguishable

GEOGRAPHICAL DISTRIBUTION AND EPIDEMIOLOGY

World wide especially in tropics in China India and Pacific Islands A disease of insanitation

ÆTIOLOGY

A lumbricoides —Large like earthworm Round tapering at both ends Mouth anterior guarded by thin lips with finely denticulated margins anus subterminal

Female —20–35 cm by 3–6 mm paired genital tubes containing uterus receptaculum seminis oviduct and ovary tubes and ducts attain length of 125 cm Total capacity 27 million eggs average daily output 200 000 2 400 eggs by one female for each gm of fæces

Male —15–31 cm by 2–4 mm yellow or brown with white longitudinal lines tail curved in semicircle two rows of tactile papillæ and two chitinous spicules

Egg —50–70 μ by 40–50 μ elliptical encased in albuminous coat with mamillated appearance stained brown by fæcal pigments

feet absence of efficient latrines Requires temperature of 75° F (24° C) for development outside body

Ætiology

Female—10–13 mm by 0 6 mm slightly expanded posteriorly vagina in posterior third Body cavity contains ovary and coiled uterine tube with eggs Maximum egg output 15–18 months after infection

Male—8–11 mm by 0 4–0 5 mm copulatory bursa at posterior end umbrella like expansion dorsal ray branches distally into small bifurcating rays two long delicate spicules—genital papillæ (Owing to situation of genital openings in both sexes worms in copula assume Y shaped figure)

General features—Two anterior cephalic glands secrete anticoagulating ferment Mouth bent dorsally buccal capsule lined with chitin contains two pairs of sharp teeth in ventral aspect of buccal cavity

Habitat—Mostly jejunum to a lesser extent duodenum not ileum Numbers at autopsy great 500–1 000 Life span 4–7 years Egg laying capacity of female 30 eggs per c c fæces *per diem* Egg count falls as worm count increases

Egg—60 μ by 40 μ elliptical transparent shell when freshly laid contains 2–4 blastomeres

Necator americanus—New World Hookworm—Resembles and produces same effect as *A duodenale* similar life history Shorter and slenderer

Geographical distribution—Not only America common in W Africa Ceylon Pacific Islands Malaya Philippines amongst aborigines of Congo and Central Africa 90 per cent of ancylostomes in tropics are of this species Also in gorilla Patas monkey rhinoceros

Female—8–11 mm by 0 4 mm

Male—7–9 mm by 0 3 mm copulatory bursa closed and blunt short dorso-median lobe appears divided dorsal ray branches at base into divergent arms with bipartite tips two separate spicules unite to form single terminal fish hook barb

General features—Sudden dorsal bend of head (esp in female) distinctive Buccal capsule smaller than in *A duodenale* irregular border in place of 4 hook like teeth ventral pair of *cutting plates* outlet of dorsal gland (*dorsal rib*) projects into oral cavity deeply placed in capsule are one pair of dorsal and one pair of submedian lancets

Egg—64–75 μ by 36–40 μ on average smaller than *A duodenale*

Ancylostoma braziliense—In dogs and cats in Brazil civet cat in Ceylon found rarely in mixed hookworm infections in India Malaya Siam Smaller than *A duodenale* Internal pair of ventral teeth smaller than those of *A duodenale*

LIFE HISTORY OF HOOKWORMS

(1) *Egg* deposited in lumen of intestine 2 4 8 blastomeres

(2) *Embryo* moves inside shell in fæces and soil gives rise to

(3) *Rhabditiform larva* which burrows into fæces feeds on bacteria At first has double œsophagus food reserves (oil globules in intestinal wall) Two moults œsophageal bulb disappears larva then leaves fæces enters earth and becomes

(4) *Infective filariform* (third stage) *larva* well-developed mouth capsule simple muscular œsophagus Moves towards oxygen supply Protected by sheath to withstand desiccation can live in damp soil (in optimal conditions) for 2 years encysts on blades of grass and may enter droplets of dew and in this manner entrance to skin is facilitated

(5) Penetrates *human skin* sheath discarded enters lymphatics gains blood stream reaches lungs on third day Then breaks through alveoli enters bronchioles and travels *via* trachea and œsophagus to stomach During migration has third moult and terminal buccal capsule is formed In intestine on 7th day has 4th moult terminal buccal capsule changed into provisional buccal capsule mouth opening directed dorsally as in adult without teeth On 15th day provisional buccal capsule is cast takes on adult form with adult buccal capsule and bursa of male In 3-5 weeks is sexually mature Ancylostome larvæ can be cultivated in Petri dish with warm water and blotting paper forming uniform layer like peasoup

PATHOLOGY

Fifty three per cent classified as hookworm disease remainder as carriers of worms Anæmia due to chronic loss of blood absorption of toxins bacterial infection of damaged small intestine Generalized œdema fat increased Effusions into serous cavities Heart liver and kidneys dilated flabby fatty Ancylostomes in numbers in duodenum and jejunum attached to bowel or in mucus Numerous small blood extravasations blood cavities in submucosa occasionally clots of blood in lumen Bone marrow hyperpla tic dominant erythropöiesis Microscopically toxic degeneration of parenchyma cells of liver hæmosiderin granules + also free iron (Prussian blue reaction)

Clinical pathology—Blood picture typical of iron-deficient hypochromic microcytic anæmia Red cells may be as low as one million average 1 400 000 Hæmoglobin may be as low as 10 per cent percentage content of hæmoglobin does not correspond to actual deficiency owing to increase of blood volume Colour index usually 0 7 may be as low as 0 5 mean corpuscular volume below normal occasional normoblasts reticulocyte count less than 3 per cent Van den Bergh reaction negative decrease in plasma protein and plasma albumin with increase of globulin Œdema due to reduction of colloid osmotic pressure Abstraction of blood by ancylostomes is important feature as is also secretion of anti-coagulant ferment Gastric juice usually shows achlorhydria and hypochlorhydria

Or in mixture	Tetrachlorethylene	min 40 (2 48 c c)
	oil of chenopodium	min 17 (1 c c)
	liquid paraffin	1 oz (29 5 c c)

in two doses of ½ oz each followed by saline purge

Hexylresorcinol much used in U S A non toxic pills or gelatin capsules 3 gr (0 2 gm) each Must be swallowed whole if chewed excoriates mouth

For adults and children over 12	5 pills
8–12	4
6–8	3
under 6	2

No food for 4 hours after treatment Alcohol contra indicated Saline purge 1 day later

After treatment —Prolonged dosage with iron (ferrous sulphate tablets) necessary occasionally blood transfusions

Prophylaxis —Contamination of soil is main factor Tea coffee cocoa banana mulberry citrus fruit and rubber plantations are serious sources and supply many carriers in small area If inhabitants defæcate under trees the conditions necessary for development are provided in the accumulation of fæces warmth moisture (dew better than rain) and shade infective larvæ are killed in a few minutes by sunlight *Latrine provision very important* shallow trench covered with soil provides good conditions (larvæ migrate vertically—rarely laterally) Heavy rain washes away fæces and is a good preventative (larvæ cannot live in water) Rise in temperature increases activity If food reserves of larvæ are used up in tropics rarely survive more than 6–8 weeks By the Chinese system of night soil preservation larvæ are killed Water supply guarded and drinking water boiled No raw fruit or vegetables should be eaten from garden fertilized by human fæces Soil should be treated to exterminate larvæ (larvæ demonstrated by Baerman method soil placed in funnel closed by rubber tube and clip with 1 mm mesh brass sieve level of water 2 5 cm above bottom of sieve Lined with cotton fabric on standing larvæ collect in rubber tube) Education in schools by diagrams and instructional films plays important part in health propaganda

Intensive mass treatment with oil of chenopodium and tetrachlorethylene is no use unless satisfactory latrines were established one year previously Bore hole latrine 16 in diameter carries risk of infecting subsoil with pathogenic bacteria it is however a method acceptable to natives and abolishes odour and flies Education of children important Cinema films have been successful in inducing people to be examined and treated

ŒSOPHAGOSTOMIASIS

Œsophagostomum apiostomum encysted under mucous membrane of large intestine produces condition like polyposis common parasite of cæcum and colon of monkeys in Africa Philippines and China In man in N Nigeria

Ovoid expansion of cuticle at anterior end limited by oral ring

Female.—10 mm. by 0 325 mm. posterior terminating in sharp point vulva in anterior half

Male.—8 10 mm by 0 35 mm. copulatory bursa with dorsal ray bifurcating into branches horse-shoe shaped structure

Egg.—60 μ by 40 μ closely resembles ancylostome in advanced stage of development

Life history.—Larva hatches from eggs in soil as unsheathed rhabditiform this is swallowed, passes through stomach and intestines and invades wall of cæcum where it forms nodules breaking out into lumen, attached to mucosa, becomes adult

Clinical features.—Dysenteric symptoms.

Treatment.—Phenothiazine effective in small doses 0 5 gms for three days

O stephanostomum closely resembles above found in man in Brazil with dysenteric symptoms.

OTHER INTESTINAL NEMATODES OF LESS IMPORTANCE

Gnathostoma spinigerum or *siamense* parasite in stomach of tiger dog and cat in India Malaya China Japan Reported in advanced larval stage in man in Siam From consuming uncooked preserved fish which contains encapsulated third stage larvæ Eggs of adult worms have been found in human fæces

Female—25-54 mm

Male —11-25 mm

Reddish in colour Globular cephalic swelling separated by cervical constriction Anterior half provided with leaf like spines

Ternidens deminutus —In man in Nyasaland Portuguese E Africa and Transvaal also in monkeys and baboons in Africa and Asia Not pathological unless in large numbers in cæcum

Female —14-16 mm by 0 73 mm genital orifice posterior and sub-terminal short vagina opens into two uterine tubes

Male.—9 5 mm by 0 56 mm copulatory bursa dorsal ray divides into two distal extremities each branch formed again and bifurcates

General characters —In appearance resembles ancylostomes anterior extremity not bent mouth capsule terminal with corona of setæ three serrated teeth guard entrance to œsophagus

Egg —84 μ by 40 μ delicate transparent resembles ancylostome in advanced segmentation

Life history —Rhabditiform larva 0 3 mm with flagellar tail hatches from egg in soil becomes sheathed and infective filariform larva (0 6-0 7 mm) Can survive desiccation reviving in water

Trichostrongylus colubriformis —Normally parasitic in upper small intestine of sheep and goat duodenum and upper jejunum of man in agricultural districts of India Persia C Africa Egypt Japan and Korea Probably quite common Eggs not infrequent in ancylostomiasis cases in India and Assam

Female —4-6 5 mm outnumbers male slender pink anterior extremity contains attentuated vulva in posterior quarter

Male —4 5 mm by 0 07 mm bilobed copulatory bursa two spicules

General characteristics —Found in mucus covering mucosa near duodenum Scraped on slide worms appear as red streaks seen against dark background on slide shaken in saline in Petri dish Mouth unarmed

Egg —63 μ by 41 μ relatively large oval thin shelled contains morula when deposited Likely to be mistaken for ancylostome translucent smaller

Life history —Eggs hatch outside body rhabditiform larvæ meta morphose into infective filariform in 6 days at 22–25° C Enter body by skin or mouth Same course as ancylostome Eastern form in Japan separated as *T orientalis* or *T probolurus* Also natural infection of gazelle and camel but rare in man Usually no symptoms may cause secondary anæmia Worms easily expelled by tetrachlorethylene 1 dr (3 75 c c)

Strongyloides stercoralis —Larval form frequently found in fæces pathogenicity doubtful confused with other nematodes principally ancylostomes Can produce condition like *larva migrans*

Geographical distribution —Almost world wide especially in tropics Brazil Cochin China In man only

Clinical —No symptoms usually—diarrhœa described also condition affecting buttocks and loins resembling *larva migrans* possibly due to migration of larvæ in the skin In infected persons aller gic urticarial eruptions due to toxins of larvæ of strongyloides Pulmonary changes also described producing bronchopneumonia

Ætiology —Adult forms parasitic in submucosa of small intestine considered to be parthenogenetic females but now claimed that parasitic male exists—shorter and broader than female resembling free living form *Real sexual cycle* carried out in fæces outside body

Female (in intestine) 2 5 mm by 0 034 mm tapering anteriorly conical tail Mouth with three lips leads to œsophagus occupying quarter of body Vulva in posterior third Prominent uterus contains 50 eggs Rhabditiform larvæ produced in 3–4 days develop into filariform infective stage and re enter definitive host via skin or buccal mucosa

Parasitic Male tail curved ventrally—two spicules and gubernaculum

Egg 50–58 μ by 30–34 μ deposited in lumen of bowel in advanced stage of development hatches immediately into embryos 0 2–0 3 mm by 0 013 mm double bulb œsophagus Passed active in fæces free living develop in 3–5 days into free living non parasitic male and female forms with rhabditiform double bulb œsophagus
This male is 0 7 mm by 0 035 mm and the female 1 mm by 0 05 mm Copulation takes place in the fæces The rhabditiform larvæ are indistinguishable from those derived from parasitic female After 3–4 days develop into post feeding mature filariform larvæ

which are the infective stage and re enter human host *via* the skin or buccal mucosa but remain alive in soil for many weeks Distinguishing feature from larvæ of *Ancylostoma* and *Necator* is œsophagus which is half the length of the body but in the latter it occupies a quarter

SCHEMATIC SUMMARY

Intestine	Female parasitic intestinal (Parasitic male ?) produces Eggs hatching in intestine
Fæces	produce rhabditiform larvæ which develop into (*a*) infective or (*b*) sexual forms which copulate and females lay Eggs
Fæces	from which emerge second rhabditiform larvæ—moult and become filari form—enter man by penetrating skin or through mouth *Migrate throu h lun͛s to œsophagus in manner similar of that of ancylostome In two weeks develop* into parasitic females in small intestine

Diagnosis—Easy by active larvæ in *fæces* Duodenal intubation more certain method Often found in diarrhœa especially sprue

In large numbers *probably cause irritation of bowel and diarrhœa* abdominal pain flatulence usually in men At autopsy found in large numbers coiled in intestinal follicles

In infected patients there is supersensitization to antigens of parasite and urticaria at site of entrance of parasite or on rubbing extracts into skin (Fulleborn) Often causes periodic urticarial eruptions in vicinity of anus and often on trunk and thighs Sometimes petechial rarely linear like *Larva migrans* Possibly due to penetration of skin by larvæ During pulmonary migration larvæ produce bronchopneumonia

Treatment.—Thioxanthone (*Miracid D or Nilodin*) specific oral dosage 5–20 mg per kg in divided doses for 6 days Short cure is 20 mg per kg for 2 days

S fulleborni parasite of monkeys has been recovered from American soldiers in S W Pacific

OXYURIASIS THREAD OR PINWORM

Oxyuris vermicularis (*Enterobius vermicularis*)—World wide (45 per cent of schoolchildren infected very common in adults in tropics)

Habitat—Lives in upper portion of large intestine especially cæcum and appendix occasionally vagina rarely ear and nose

Small white thread like mouth surrounded by cuticular expansion (halo) skin transversely striated the only nematode in man with double bulb œsophagus in adult

Male —Seldom seen 2 5 mm much smaller and does not migrate like female Posterior third curved spirally caudal extremity blunt six sensory papillæ single spicule 70 μ

Female —*9–12 mm* long pointed tail anus 2 mm from posterior extremity

Egg —*50–54 μ* by *20–27 μ* *flattened on one side* colourless double contour shell bean shaped contains almost fully formed embryo

Life history —No multiplication of worms in body Fertilized female migrates out of anus deposits eggs in natal folds After a few hours embryo develops and grows to 140–150 μ Taken into mouth generally under finger nails it hatches in digestive juices Larvæ pass after two moults from small into large intestine where they become mature Duration of cycle two weeks

Retrofection described by Schüffner in which infective larvæ re enter the anus

DIAGNOSIS

Cellophane N I H swab makes it possible to scrape eggs from perineum and recognize them under microscope Females may be seen outside anus at night Occasionally eggs found in fæces Does not cause eosinophilia Number infecting host determined by number of eggs swallowed Scotch tape method by which ova adhere to surface found useful and simple

CLINICAL FEATURES

Mature worms penetrate mucosa encyst in submucosa of large intestine or appendix and cause appendicitis in 2 per cent found *in lumen* Nasal itching common also pruritus ani *Familial infections* common

TREATMENT

In adults may be difficult For *pruritus* ung hydrarg ammon to anus Raw carrot diet cut down sugars and carbohydrates Great many remedies

Hexylresorcinol —In U S A *by enema* 1 2 000 solution after soap and water enema 2 pints to adult and to limit of tolerance in children One every 3 weeks No better results when taken by mouth

Piperazines —Recent discovery in Antepar (piperazine hydrate in *syrup (150–70 mg per kg per day)* and Entacyl (piperazine adipate) with mild aperient—syrup of figs or senna (see p 247) Threadworms often disappear after a barium *meal The barium* finds its way into every crevice of the intestine *Barium sulphate* in 75 per cent concentration in six ounce meal of umbrose a second dose is taken 3 hours later and followed by calomel The process is repeated next day The dose for children is three quarters that for adults

Prophylaxis —General measures Sleeping in cotton drawers cotton gloves paring finger *nails* and washing hands after defæcation

TRICHURIASIS "WHIPWORM"

Trichuris trichiura (Trichocephalus dispar).—Distribution world wide more in tropics than elsewhere in many countries 50 per cent of population infected Produces no special symptoms Identical with species in pig

Male.—30–45 mm attenuated portion contains cellular œsophagus half as long again as thicker posterior portion Caudal extremity curved ventrally Single spicule in sheath studded with spines

Female.—30–50 mm anterior attenuated portion twice as long as posterior which is occupied by stout uterus and eggs Females preponderate to male 466 1

Egg.—50 μ by 22 μ characteristic barrel shape brown single shell with plug at each end unsegmented embryo

General characteristics.—Greyish white or pink Lives in cæcum maintains position by transfixing fold of mucous membrane by slender neck

Life history.—Spread by stale fæces Eggs unsegmented embryo develops slowly attaining full length in 6–12 months Can withstand low temperature owing to thick shell and lie latent for 5 years Development direct Embryo hatches when egg is swallowed egg shell digested by intestinal juices Larva passes to cæcum or colon adheres to mucosa becomes adult

CLINICAL FEATURES

No special pathology Some claim it causes diarrhœa Has been seen in mucosa by sigmoidoscopy in rectum may cause rectal prolapse in children

TREATMENT

Difficult to expel Worms may be very numerous Recent report of over 1 000 removed

Piperazines.—Recently found effective such as —

Entacyl (Piperazine adepate) The hydrate salt not recommended
Two tablets (300 mg) three times daily Up to 6 years 1 tablet for each year of life for week or ten days In syrup form more suitable for children

Hexylresorcinol 1 2 000 solution advocated Bowels first cleansed by soap and water enema and 2 pints of former for adult less for children injected one enema weekly for three

Warm hydrogen peroxide solution (1 5 per cent) gradually introduced into intestine removes these worms

Capillaria hepatica (Trichocephalus hepaticus).—Closely allied to *T trichiura* normally parasite of liver of rat where eggs are deposited in masses Life cycle like *T trichiura*

In British soldiers in India Septic pneumonia secondary to abscess of liver caused by adult worms Eggs in liver substance not in fæces

TRICHINIASIS

Trichinella spiralis—White worm just visible to ey

Distribution—World wide Formerly common in Germ France now in U S A China Syria India (from ea pigs) Algeria E Africa *Rare in Australia* Out England and S Wales from eating sausages Pigs bears rats commonly infected Laboratory animals lizards capable of infection Birds refractory Infe mally from pig to rat rat to rat (sick rats eaten carni Man not normal intermediary

Male—*1–6 mm* by *0 04 mm* cloaca posteriorly between t appendages two pairs of papillæ

Female—3–4 mm by 0 06 mm vagina in anterior fifth posterior half anterior occupied by coiled uterine tu terminal

Egg—20 μ in upper uterus embryo soon breaks loose and in uterine cavity

Viviparous embryos voided into lumen of intestine 100 μ by 6

Habitat—Small intestine embryos emitted by female mig muscles where they *encyst* Cysts *very small* cannot by meat inspection unless by microscopic examination calcified Male dies after copulation female 5–6 wee discharging hundreds of embryos

Life history—Embryos travel by lymphatics and veins pie of vessels encyst in striated muscles—diaphragm inte laryngeal and tendinous insertions

CLINICAL FEATURES

Stage of invasion—Symptoms resemble cholera and dysente hyperpyrexia (T *104–106* F) *During migration* o through tissues typhoidal symptoms with remittent T m delirium muscular pain leucocytosis and high eosinoph

Stage of deposition—Encystment in muscles in 3 weeks p cachexia *toxic absorption* œdema of face abdomen an pruritus skin eruptions Blood and albumin in urine occas

Terminal stage—Death usually *in second stage* Recovery resolves but muscular pains persist Moderate eosinophi

DIAGNOSIS

Eosinophilia very high *in acute stage* *may be 60–90 per* decreases in chronic absent after 9 years Adult worms and e in fæces *In chronic rheumatoid stage* cysts identified under scope by biopsy when calcified by X rays At autopsy fc pectoral diaphragm laryngeal muscles best method diges 50 gm muscle by artificial gastric juice In living subject portion taken by biopsy can be treated similarly

Subclinical trichiniasis in 1 per cent of population of Great Britain

Precipitin test with extract of parasite positive too late

Intradermal test antigen from artificially infected rabbit muscles Immediate and delayed reactions

TREATMENT

No specific Intravenous calcium gluconate in stage of invasion Injection of convalescent serum controls toxic features Subcutaneous injection of *cariasept* (preparation of thymol) in olive oil has given some results in U S A Parathyroid—vitamin D—calcium treatment aims at calcification and death of parasites

Prophylaxis —Destruction of rats inspection of pork especially sausages Prohibition of bear meat (U S A Russia) Areas with highest proportion of garbage disposal to pigs give highest trichiniasis rates

FILARIASIS

Group of diseases due to invasion of lymphatic system or connective tissues by nematode worms—Filariidæ—producing living embryos in blood or tissues and conveyed by biting insects

1—*Wuchereria bancrofti* (*Filaria bancrofti*)

Most important produces most profound pathological changes

GEOGRAPHICAL DISTRIBUTION

Wide tropical and subtropical North to Spain in Europe Charleston U S A south to Argentine Transvaal Queensland Isolated foci in N and Central Africa Egypt W Indies Brazil Venezuela Guianas S China India Ceylon E Indies Pacific Islands

ÆTIOLOGY

W bancrofti thread like white worm in lymphatic vessels and glands thoracic duct Sexes coiled together can be separated with difficulty Dead individuals become cretified

Male —40 mm by 0 1 mm coiled with corkscrew like tail two spicules (larger 500 μ) short thick proximal and whip like distal portion ending in hook shorter (200 μ) grooved on ventral aspect fifteen pairs of minute sensory caudal papillæ and saddle shaped thickening of cuticle on posterior wall of cloaca

Female —65–100 mm by 0 2–0 28 mm anterior end tapers ending in swelling Rows of sessile papillæ on head oral aperture leading to cylindrical œsophagus median intestinal tube one-third to one fifth of diameter opens into rectum posteriorly Tail narrow abruptly rounded Vulva 0 8 mm behind anterior end uterus divided into two branches much coiled occupying greater portion of body two ovaries and ducts extend to within 1 mm of tail Eggs in upper uterus enclosed in chorionic membrane which becomes sheath of living embryos (microfilariæ) These are emitted by viviparous female and travel *via* lymphatics into blood stream whence they are ingested by mosquitoes

Embryo (microfilaria) —280 μ by 7 μ when seen in living state is structureless details shown when stained Entire embryo enclosed in sheath permitting of forward and backward movement Longer than embryo collapsed part trails behind Middle third contains granular material in primitive intestine *Innen korper* Transverse muscular striation one fifth length from head V shaped opening Anterior V spot =Excretory pore Short distance from tail is second pore (Posterior V spot) representing anus or cloaca In stained specimen body of embryo is composed of closely packed nucleated cells which stop short of tip of tail Head end covered by prepuce from which a fang is shot out by living embryo

Microfilariæ pass with difficulty through peripheral capillaries less active in day than in night blood capable of movement and can travel from place to place

W bancrofti var *vauceli* —New variety W coast Madagascar Microfilaria shorter 250 μ absence of two terminal nuclei in tail shorter cephalic space genital cells larger longer excretory pore granular inner body less graceful curves in posture

Filarial periodicity —Microfilariæ exhibit *nocturnal periodicity*—*i e* in peripheral blood in larger numbers in night than in day (W Indies S America N Africa and China) Maximum concentration 10 p m–2 a m In day time maximum number microfilariæ in lung capillaries Mechanism of periodicity never satisfactorily explained Numbers influenced by sleeping diminish on waking and bodily activity Reversal of periodicity can be obtained in three days by reversing hours of sleeping and waking

Nocturnal unsheathed microfilaria now found in monkey (*Cercopithecus*) by Hawking periodicity like that of *W bancrofti* in man

Life history —Within one hour of entering mosquito s stomach microfilariæ cast sheath bore through stomach wall collect at anterior end of stomach and enter cylindrical portion of mid gut Forward transportation effected by reversed peristalsis Proboscis of mosquito exerts positive chemotaxis on microfilariæ Mosquito abstracts 10 times number of microfilariæ present than in equal quantity blood

Microfilariæ enter muscles of thorax and lie between muscular fibres Within two days they increase in girth the anal pore enlarges and the excretory vesicle becomes prominent Nuclear proliferation takes place then becomes squat sausage form tail absorbed Mouth and œsophagus apparent from 5th day

Larva 0 5 mm with bulbar œsophagus elongated and worm like moves sluggishly three caudal papillæ function in progression and facilitate penetration of human skin On 10th day larval filaria 1 4 mm travels forward to head enters proboscis sheath found occasionally in abdominal cavity and legs of mosquito Two or more ecdyses In high temperature and moisture development is complete in 10–14 days retarded by cold to six weeks Sometimes die in thoracic muscles when enclosed in chitin like

mummy When infected mosquito bites man larvæ attracted by warmth break through terminal portion of proboscis sheath (Dutton s membrane) wriggle onto skin and penetrate puncture caused by stylet of mosquito

Intermediary hosts—Complete development of *W bancrofti* in *Culex fatigans* (W Indies India Philippines) *C pipiens* (China) various other species of Culex in lesser degree—*Mansonioides annulifera* (S India) *M africanus* (Central Africa) *Aëdes togoi* and *A chemulpœnsis* (Japan) various species of anopheles in S India China N and W Africa Dutch E Indies and Queens land

Non periodic variety of *W bancrofti* in Pacific (*W bancrofti* var *pacifica*) In Pacific Islands this form of filariasis universal but also rarely non periodic filaria in Philippines (possibly also S Sudan) Microfilariæ and adults morphologically similar to *W bancrofti* but microfilariæ in blood in equal numbers by night and day Does not develop readily in *C fatigans* but in *Aëdes scutellaris pseudo scutellaris A polynesiensis* and *A fijiensis*

2—*Wuchereria malayi*

GEOGRAPHICAL DISTRIBUTION

Malaya Dutch E Indies Central India Ceylon S China Korea Indo-China

ÆTIOLOGY

W malayi—Practically identical with *W bancrofti* females indistinguishable In male differences in tail papillæ Spicules more delicate also lack of transverse corrugations on stout portion of spicule

Microfilaria quite distinct from that of *W bancrofti* 200–250 μ by 5–6 μ nocturnal periodicity like that of *W bancrofti* on E coast of Malaya non periodic on W Chief points of distinction different posture and enlongated nucleus at tip of tail Lies closely folded with head close to tail irregularly disposed showing major curves and minor angulations Nuclei blurred and intermingled Tail tapers to fine point cephalic space twice as long as broad Excretory pore and cell separated Develops in special mosquitoes of genus *Mansonioides* crepuscular or nocturnal feeders Development similar to *W bancrofti* terminal nuclei can be distinguished in larva more rapid 6–8½ days No development in *Culex* although may complete metamorphosis in species of anopheles but principally *Mansonioides annulatus M annulifera M longipalpis M uniformis*

Pathological effects same as *W bancrofti* produces mainly elephantiasis of legs

Prophylaxis—Eradication of water plants in which mansonioides larvæ develop is effective

Relationship to W bancrofti—Exist together in S India and Malaya *W bancrofti* urban distribution *W malayi* rural

Pathology of non periodic *W bancrofti* **and** *W malayi* —Similar former may produce elephantiasis of arm latter of legs

CLINICAL FEATURES

Varied manifestations lymphangitis filarial abscess arthritis (hip joint) synovitis varicose groin or axillary glands lymph scrotum orchitis funiculitis hydrocele chylous hydrocele elephantiasis of legs scrotum vulva arm mamma and other parts chylous diarrhœa Retroperitoneal *suppuration* (*filarial abdomen*) may be fatal General tendency to superinfection with pyogenic streptococci leading to septicæmia and death

Ascending lymphangitis —Common early sign of filarial disease red *streaks usually in legs cord like swelling of lymphatic vessels* and glands Usually rigor pyrexia pain headache vomiting lasts for several days Internal lymphangitis produces same train of symptoms and rigor—often mistaken for malaria Retroperitoneal lymphangitis simulates acute abdomen Liable to secondary streptococcal infection Recurring attacks predispose to lymph stasis and eventually to elephantiasis and elephantoid *fever*

Filarial abscess —Adult filaria may be injured or die as result of *lymphangitis becomes secondarily infected forms nucleus of* abscess generally deep seated in muscle but often at site of lymphatic glands of groin axilla or epitrochlear region Dead filariæ often found in abscess cavity

Varicose groin glands —*Commonly with* lymph scrotum and chylous ascites or chyluria Enlarged hard fibrotic inguinal glands in bed of distorted varicose lymphatics usually transmit impulse on *coughing*—not to be mistaken for femoral hernia Often associated with funiculitis and filarial hydrocele Puncture of glands and aspiration of lymph reveals microfilariæ Filarial varices *on* abdominal surface axilla legs arms and spermatic cord often contain live adult filaria

Glandular enlargement —Especially associated with non periodic Pacific *form* There enlargement and fibrosis of epitrochlear glands common

Lymph scrotum —Skin silky to touch contains number of lymphatic varices which exude lymph often with microfilariæ Associated with enlarged inguinal glands

Chyluria —Result of rupture of lymphatic varix into bladder *chyle* in urine which is milky contains 1 8–2 6 per cent of fat albumin fat globules lymphocytes and often microfilariæ and blood (hæmatochyluria) Associated with periodic *W bancrofti* rarely with non periodic form *Chyluria attended* with suprapubic oppression pain and general debility

Lymphuria —Due to lymphatic *obstruction* in renal tract by calcified filariæ Urine cloudy contains lymphocytes and albumin

Chylous hydrocele and hydrocele fluid often contains microfilariæ Other signs of filarial disease present

Filarial orchitis—Acute onset usually with epididymitis and hydrocele pyrexia rigor and leucocytosis

Filarial synovitis—Hip or knee with pyrexia pain adenitis very often secondary suppuration

Septic complications—Usually streptococcal common accompaniment of filarial lesions may result in septicæmia

Filarial elephantiasis—Most frequently in heavy filariated countries Ninety five per cent of legs and scrotum less frequently arms mamma vulva Usually result of repeated attacks of lymphangitis Calcified filariæ in deeper tissues demonstrated by X rays Lymphatic glands draining area enlarged Elephantiasis of scrotum may attain enormous proportions and incapacitate patient

DIAGNOSIS

By discovery of microfilariæ in blood (thick drop method) not always present in advanced filarial disease Knott s method venipuncture 1 c c blood in 9 c c of 2 per cent formalin in distilled water centrifuge microfilariæ in deposit By eosinophilia 15-20 per cent By lymphatic gland puncture (p 26) microfilariæ in lymph Section of gland at biopsy demonstration of dead or calcified filariæ

Complement fixation test as in schistosomiasis (p 196) antigen prepared from dog filaria *Dirofilaria immitis*

Intradermal test—0 25 c c of 0 1 per cent extract of *D immitis* as antigen Immediate and delayed reactions more reliable for *L. loa* than for *W bancrofti* infections Not reliable in later stages of filarial disease or in elephantiasis

TREATMENT

Hetrazan (*Banocide*) (1-diethylcarbamyl 4 methyl piperazine hydrochloride) exerts an immediate action upon the microfilariæ in the blood circulation though it does not affect those in closed cavities of the body such as hydroceles Hawking thinks that is opsonizes the microfilariæ which are subsequently devoured by leucocytes The evidence now is considerable that it banishes microfilariæ periodic and non periodic from the bloodstream for as long as six months It has still to be proved that its effects are permanent or that in the long run it destroys the parent filariæ So far the evidence is unsatisfactory Regardless of dosage a marked reduction of microfilariæ in the blood results within the space of 2-4 days Side reactions are few headache nausea vomiting and sometimes skin rashes In Virgin Islands 90 6 per cent reduction claimed The dose is about 2 mg per kg three times daily for three weeks The maximum dose is about 300 mg for an adult male daily but 150 mg daily also appears to be efficacious When injected intramuscularly microfilariæ disappear from the blood within a few minutes

Cortisone in advanced elephantiasis Improvement is due to anti inflammatory action of drug in reducing lymphatic blockage In most cases it is advisable to apply bandage therapy with the addition of Unna s paste which has the advantage of reducing the œdema The dose advised is 100 mg daily in divided doses over a period of 30 days or longer Total period of treatment 7–10 months

Lymphangitis —Rest cooling applications injections of adrenaline (1 1 000) relieve pain and alleviate condition Recently good results reported from sulphapyridine and proseptacine treatment

Chyluria —Rest in bed foot of bed elevated wash out bladder with *boracic acid* introduce into bladder styptic solution —

Liq adrenal 1 1 000	1 oz (29 5 c c)
Zinc sulphat	5 gr (0 324 gm)
Lot acid boric ad	10 oz (295 c c)

Operative measures —Reserved for elephantiasis *N B* —Varicose groin glands must not be removed or lymphous fistula and *elephantiasis result*

Elephantiasis of leg —Elevation of limb elastic bandage *Lang s operation* deep lymphatic drainage, stripping periosteum of femur bone trephined strips of fascia inserted *Kondoleon s operation free incision into fascia lata removal of strips* of aponeurosis often temporarily successful

Elephantiasis of scrotum —Removal of scrotum elastic webbing applied to express blood penis exposed Testes and cord separ ated hypertrophied gubernacula divided Results successful generally no recurrence mortality less that 5 per cent

Elephantiasis of arms —*Removal of strips of tissue*

Elephantiasis of mammæ —Removed successfully

Drug treatment —Disappointing Recently intramuscular injections of anthiomaline recommended (see p 197) also injected into enlarged glands Good results claimed in arresting elephantiasis Effect on microfilariæ not demonstrated

Prophylaxis —General anti mosquito measures and DDT mosquito nets In Pacific Islands clearing undergrowth and creating a through draught blows away mosquitoes In Malaya and S China clearing plants in waterways—especially *Pistia stratiotes*—success ful Subjects of filariasis with microfilariæ in blood are a danger to community

LOA LOA FILARIASIS (Loasis)

Mostly in W Africa parasite of connective tissue characterized by Calabar swellings and appearance of *filariæ under skin and in con junctiva of eye*

GEOGRAPHICAL DISTRIBUTION

W Africa Sierra Leone to Angola especially the Cameroons in rain forest mostly along courses of big rivers far inland up Congo 1 500 miles also S Sudan (Bahr-el Ghazal)

ÆTIOLOGY

Loa loa Eye worm Stouter than *W bancrofti* with chitinous bosses on cuticle more numerous in female Mouth unarmed no papillæ When dead often becomes cretified Embryo maintains diurnal periodicity in blood in contrast to nocturnal periodicity of *W bancrofti* Loa loa found also in forest monkeys of the rain forest in Cameroons Some of these are identical with that of man and are transmissible to him Others are not Seemingly a biological problem comparable with that of *W malayi* (see p 222)

Male —30–34 mm by 0 35–0 43 mm tapers to tail which curves ventrally with two lateral expansions of cuticle Ano genital orifice 0·08 mm from tail tip with two unequal spicules four globular pedunculated papillæ one pair small postanal papillæ

Female —20–70 mm by 0 5 mm posterior attenuated broadly rounded Vulva 2 5 mm from anterior extremity Two long uterine tubes contain eggs in all stages Reproduction ovo-viviparous Embryos develop within egg envelope and uncoil themselves on expulsion from vagina

Embryo (microfilaria) —298 μ by 7 5 μ in fresh blood impossible to distinguish from microfilaria of *W bancrofti* in stained films assumes stiff angular attitude tail disposed in series of sharp flexures nuclei of central column of cells larger and extend into tip of tail Large genital cell at beginning of posterior third Strictly diurnal inversion of periodicity effected gradually as on voyage round world Sometimes embryo not found in blood for 6–7 years from date of infection

Life history —Stages similar to those of *W bancrofti* in thoracic muscles connective tissue and fat body of blood-sucking day biting mangrove flies *Chrysops silacea* and *C dimidiata* *C centurionis* and *C langi* in Cameroons *C distinctipennis* in Sudan Development complete in 10 days then 2 mm by 0 025 mm Three ecdyses Larvæ congregate in head in large numbers at root of proboscis sheath when fly feeds then enter skin as in *W bancrofti* In S Nigeria 3 5 per cent wild chrysops naturally infected In human host larva enters connective tissue and migrates Development very slow may be several years Adults numerous in body long lived (17 years)

Intermediary hosts —*Chrysops* Blood sucking fly females attack warm blooded animals males live on vegetable juices Eyes large in female contiguous in male Antennæ consists of three dissimilar segments Venation of wings complex Second longitudinal vein not forked , markings and blotching of wings Thorax usually irridescent Semi aquatic in breeding habits eggs laid

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near water Larvæ slender cylindrical in water Pupæ like those of Lepidoptera *Chrysops dimidiata* very abundant in W Africa (Nigeria Cameroons) Face and palpi yellow thorax black with yellow stripes Abdomen and legs yellow and dusky brown Distal half of wings smoky *C silacea* as above but with abdomen red or bright orange

PATHOLOGY

L loa migrates to subcutaneous tissues under skin especially conjunctiva attracted by warmth No marked blood changes except eosinophilia which is persistent marked 30–60 per cent

CLINICAL FEATURES

Mainly due to migrations of adults pricking and creeping sensations Calabar swellings—diffuse œdematous swellings of arms legs and face Allergic (reproduced by injection of extract of worms) evanescent recurring at regular intervals sometimes accompanied by appearance of worm under skin *Microfilariæ may or may not be found in blood* Cyst like swellings sometimes contain adults Found at operation for hernia etc Worms in eye cause conjunctivitis photophobia and irritation Urticaria pruritus and allergic papular dermatitis sometimes

DIAGNOSIS

By microfilariæ in blood (thick drop) usually numerous also eosinophilia complement fixation and intradermal tests as in *W bancrofti* latter usually more marked (see p 225)

TREATMENT

No specific treatment Palliative to Calabar swellings reduce by evaporating lead lotion Desensitization by injections of filaria antigen (made from *Dirofilaria immitis*) extract in saline Removal of adult worms from conjunctiva under novocaine anæsthesia (*Does not* necessarily remove infection)

Hetrazan (see p 225) has given more satisfactory results in this than in any other form of filariasis In several instances the adult loa parasites have been found dead or partially cretified under the skin after a course of treatment and Calabar swellings have subsided but in others they have returned The dose given by the mouth for 7–11 days in doses of 3–6 mg per kg The initial dose on the first day should not be less than 3 mg per kg The *total amount of hetrazan in an adult man ranges between 17 and* 26 gm

OTHER FILARIÆ

Mansonella ozzardi (Filaria ozzardi)

W Indies S America N Argentine amongst aborigines (now considered identical with *F demarquayi*) adult found in omental tissues

Male —32 mm tail coiled one spicule

Female —65–81 mm by 0 25 mm two prominent papillæ on caudal extremity terminal thickened cuticle

Microfilaria —173–240 μ by 4–5 μ closely resembles *A perstans* but has sharp tail

Life history —Intermediary insects are midges *Culicoides furens* and *C paraensis* Microfilariæ develop in thorax 7–8 days larva in proboscis 0 78 mm two ecdyses (For description of Culicoides see below)

Acanthocheilonema perstans (*Filaria perstans*)

In man and chimpanzee Central Africa Gold Coast Sierra Leone Nigeria N Rhodesia Uganda Venezuela Trinidad Guianas N Brazil and N Argentine in association with banana plantations In West Africa commonly associated with *L loa* Adults long cylindrical smooth Tail incurved in both sexes chitinous covering gives mitred appearance In mesentery perirenal tissue and pericardium Causes no tissue possibly allergic reactions

Male —45 by 0·06 mm head 0·04 mm in diameter cloaca with pre-anal and postanal papillæ Two unequal spicules

Female —70–80 mm by 0 12 mm head club shaped vulva 1 2 mm from head

Microfilaria —Unsheathed contractile measurements vary 90–110 μ by 4 μ Small microfilaria with abruptly rounded tapering tail extending two thirds of length Locomotes freely in blood in heart lungs aorta and large vessels

Life history —Develops in midges *Culicoides austeni* and *C grahami* Development in thoracic muscles as in *W bancrofti* in 6–7 days larval filaria (0 7 mm) emerges from proboscis Seven per cent of wild-caught midges infected in endemic areas

Clinical features —Nil

Treatment —Hetrazan has some effect upon microfilariæ perstans in doses of 5 mg per kg but reports conflicting

Culicoides —Small blood sucking gnats Antennæ plumose in male pilose in female but long and thread like Bite voraciously at dusk or night Wings contain pigment in membrane not scales Eggs laid in shallow water Larvæ red blood worms with four pairs of gills feed on algæ Adult emerges in 3 days

Dipetalonema streptocerca formerly known only from the microfilariæ which was named *Agamofilaria streptocerca* It is probably a parasite of the chimpanzee and the adults are present in the connective tissues and are closely related to *A perstans* The microfilariæ (215 μ in length) are found in the corium of the skin and are distinguished by the walking stick handle of the tail extremity and by four prominent nuclei there Develops in *Culicoides* sp and is susceptible to hetrazan

ONCHOCERCIASIS

Onchocerca volvulus blinding worm Filaria parasite producing nodules in skin often eye lesions and blindness

GEOGRAPHICAL DISTRIBUTION

W Africa (Sierra Leone to Angola) Congo N Kenya S Sudan Tanganyika Mexico Guatemala C America mostly in well watered districts in vicinity of trees and forests In Guatemala on coffee plantations 3 000 ft

ÆTIOLOGY

O volvulus (*Filaria volvulus*) white filiform with cuticular striations tapering at both ends female longer four males and two females in every tumour

Male—20–40 mm by 0 2 mm Tail is slightly spiral bulbous at tip Two pairs of pre anal post anal and intermediate papillæ two unequal spicules one with fluted end

Female—60–70 cm by 0 4 mm Head round truncated tail curved cuticular striations not so marked as in male ovo-viviparous

Egg—With striated shell pointed process at each end (like oranges *wrapped in tissue paper*) *30–50 μ*

Microfilaria—*300 μ by 8 μ sheathless In fluid cyst-cavity lymph* glands surrounding skin very rarely in blood Often in healthy skin in vicinity of eyes and in cornea Two types larger and smaller Body tapers and ends in sharply pointed recurved tail Thickening of cephalic cone at commencement of nuclear column

Life history—Development in simulium buffalo gnat Abstracts *microfilariæ from deep layers of skin near nodule they enter* stomach pierce walls and pass to thoracic muscles where they develop for 7 days Larva with two caudal papillæ 0 45–1 mm then found in proboscis Simulium day biting fly 2–6 per cent naturally infected in endemic areas in Africa 11 per cent in Guatemala

C Africa *S damnosum S neavei*

C and S America { *S avidum* / *S ochraceum* / *S mooseri* }

Simuliidæ—Small black flies 1–8 mm with blade like piercing mouth parts in female Characteristic is *prominent* hump caused by development of scutum reduction of prescutum Antennæ 10–11 joints In female eyes separated *closely set and prominent* in male Wings broad iridescent Distinct *alulæ* Found in enormous numbers in favourable localities in spring and early autumn Breed in running water Eggs laid in masses larvæ in 2–3 weeks Attach themselves to stones weeds etc Controlled by DDT Complete success obtained in Leopoldville and also in Kenya where larvæ of *S neavei* are transported attached to crabs (*Potamon niloticus*) phoretic association

PATHOLOGY

Peculiar subcutaneous fibrous tumours size of pea to pigeon's egg. One or several on parts of body in which lymphatics converge: axilla, popliteal space, elbow, suboccipital region and intercostal spaces. Considerable pain. In S. America in occipito-frontal and temporal regions in association with eye symptoms. Tumours on scalp measure 6–30 mm., easily enucleated. Dense mass of connective tissue mostly made of coiled up bodies of females embedded in stroma. May give rise to neoplasm. Usually without symptoms, but may produce epileptiform attacks.

Lymphatic enlargement of the scrotum, hydrocele, enlarged testes and elephantiasis of legs reported with microfilariæ in skin. Elephantiasis of scrotum less œdematous than that of *W. bancrofti*. Acute arthritis reported with microfilariæ in synovial fluid.

Skin rashes.—Erysipelatoid rashes (*Erisipela de la costa*). Common in C. America: xeroderma, lizard skin, lichenoid eruption especially in Europeans; skin thickened and wrinkled, causes peculiar enlargement of pinna of ear. Deep-seated onchocerca nodules found usually but not always.

Eye lesions.—Microfilariæ in cornea and choroid (corneal microscope). Keratitis punctata typical; photophobia, xerosis, impaired vision, ultimately complete opacity (pannus) of cornea and blindness. *Usually associated with erysipelatoid inflammation* of face, neuralgia and pyrexia. The greater the distance between the eyes and location of adult filariæ the later will eye lesions develop.

DIAGNOSIS

Biopsy of skin: saline solution, centrifuge at 37° C., demonstration of microfilariæ in deposit; also in scrapings of skin by Thiersch razor. Blood: moderate eosinophilia. Excise tumour and cut section to show adult onchocerca. Intradermal and complement fixation tests as for *W. bancrofti*.

TREATMENT

Excision of tumours: denodulization in early stage said to arrest progress of eye or skin symptoms. Intravenous injections of neostibosan as for kala azar have been tried (see p. 27) but results inconclusive. *Hetrazan* used in Mexico and Guatemala on the whole with good results; the great drawback being the serious character of some of the side reactions due to the destruction of microfilariæ in the skin. Herxheimer-like reactions have been recorded with large doses although the embryos rapidly disappear from the skin; no proof has as *yet been forthcoming upon its effects on the adult onchocerca* which apparently escape unscathed. *Antrypol* (suramin) more suitable than hetrazan. Total dosage 160 mg. per kg. or 1 gm. at weekly intervals for 10 doses. Thought to be lethal to adult worms. Combined treatment—preceded by hetrazan 6 mg. per kg. daily for 28 days. *Antihistamines* and *cortisone* applicable for allergic reactions.

DRACONTIASIS—GUINEA WORM

(Dracunculus medinensis)

Common parasite of man in India Persia Arabia Sudan W Africa (especially Gold Coast) N Rhodesia West Indies Brazil Guiana Common parasite of carnivora in Africa in N America in fox racoon and mink but not in man

ÆTIOLOGY

Female—*Dracunculus medinensis* two feet in length thickness of knitting needle (32 5 cm by 1 5–1 7 mm) Lives in connective tissues harmless till parturient Geotropism drawn to earth—*to fingers toes scrotum female breasts* 90 per cent migrate to feet (external malleolus) Body cylindrical smooth white Tip of tail pointed forming blunt hook Head rounded terminating in thickened cephalic shield Single-bulbed œsophagus Worm mostly occupied by double uterus containing embryos Double ovary at posterior extremity Secretion from head glands irritating blisters skin Vulva is small tube in centre of worm When douched with water contraction forces uterine contents forward thickened cuticle gives way and cap is blown off Uterus then extruded bursts and viviparous embryos are shed into water Worm then dies often becomes cretified but sinus containing dead worm becomes septic may coil round tendons and break

Male—Very scarce has never been found in man but in experimental dog 2 1–2 9 cm equal spicules 490–730 μ Lives in between muscle layers of groin Copulates in deeper tissues then dies

Embryo—651–750 μ by 17 μ Transverse striation of cuticle flattened long slender tail rounded head bulbous œsophagus Two glands at root of tail In water does not swim but coils up with side to side lashing of tail and tadpole movements of body In water 6 days in mud 2–3 weeks then swallowed by water flea *Cyclops* when coiled up—*Cyclops quadricornis* or allied species Jerky movement of embryo attracts cyclops (*like trout* and fly) Tail penetrates gut wall migrates into body cavity feeds on ovary or testes of cyclops 2–3 ecdyses Then tail absorbed cylindrical posterior extremity trilobed 4–6 weeks development Cyclops then swallowed by man Cuticle dissolved by gastric juice larva emerges Development into adult occupies one year

Epidemiology—Limited to certain localities by species of cyclops wells etc (well water frequently in Indian villages 38 per cent. cyclops infected) Rhythm of infections one to two months in year January and February in Gold Coast (Ghana) Infected cyclops *lie at bottom of well therefore* more people infected in dry season when wells are partially empty

PATHOLOGY AND CLINICAL SYMPTOMS

Female guinea worm travels to feet and parts of body in contact with water in water carriers of India appears on back May die at any stage cause sterile abscess or become calcified Appearance on surface of body preceded by allergic symptoms fever and urticaria vomiting diarrhœa (Similar symptoms produced by injection of extracts of worm) Cellulitis as result of injury to or rupture of worm œdema secondary streptococcal invasion arthritis synovitis epididymitis tendinous contractions ankylosis of joints ensues Guinea worms found at operation in hernial sacs etc Leucocytosis in early stages of infection in allergic stage marked eosinophilia later may be none

DIAGNOSIS

Worms seen or felt under skin Injection of 10 per cent collargol renders them opaque and visible by X rays When calcified easily demonstrated Eosinophilia

Intradermal test with extract of dried worm gives positive wheal with outrunners

TREATMENT

Native custom make worm protrude from aperture in skin by douching and then gradually wind out on stick requires time and patience worm usually ruptures and cellulitis results When located by X rays can be dissected out

Bichloride of mercury method —Aspirate blister fluid with syringe worm injected under skin with 1 1 000 bichloride of mercury solution gradually dies and can be extracted gradually Injection of 9 min of 1 1 000 adrenaline prevents allergic symptoms

Specific treatment —Phenothiazine specific for *D medinensis* Injected in oily solution 4 gm (61 6 gr) intramuscularly at weekly intervals Two courses sufficient Finely powdered phenothiazine is emulsified with adeps lanæ and olive oil Each injection consists of 10 c c of the emulsion (phenothiazine 1 gm) at body heat at some distance above and below site of the worm—two on extensor and two on flexor aspect (if in leg) Site of injection massaged for 5 minutes Sites are anæsthetized by injection of 3 per cent novutox (procaine and adrenaline solution) At least 1 gm (15 4 gr) of phenothiazine injected in vicinity of buried worm After 5–7 days the worm may be extracted by rolling stick method In massive induration or sinus injection is made directly into area Sinus dries up and worm massaged out by pressure No toxic symptoms noted Penicillin for secondary infections

Prophylaxis —Protecting wells or drinking water from pollution by guinea worms Adding potash to water or raising temperature by portable steam generator kills cyclops In Mysore where step wells are source of infection introduction of barbel fish which feed on cyclops has been effective Wells also treated every 14 days with *perchloron* (bleaching powder substitute)

CHAPTER XV

METAZOAL DISEASES

CESTODES (Tapeworms)

Communal segmented worms Head develops independently from embryo Segments = strobila musculature relieves strain on head Each segment (proglottis) hermaphroditic male elements fertilize female of adjacent segment former develop first Nutriment absorbed through cuticle Live for several years

1 **Pseudophyllidea,** with slit like suckers and grooves (bothria)

"BROAD TAPEWORM"

Diphyllobothrium latum Dibothriocephalus latus

Geographical distribution —In small intestine of man dog cat bear walrus sea lion fox mongoose mink pig Sweden Russia other European countries Turkestan Japan Madagascar Central African lakes recently U S A (L Michigan)

Ætiology —*D latum* long broad flat tapeworm grey translucent may attain 10 metres Coiled in small intestine Scolex 3 mm two slit like suckers thin neck 3–4 000 proglottides Genitalia complicated rosette shape twisting of uterus Dorsal aspect contains main male elements ventral female No segments passed in fæces

Egg —*Brown operculated 70 μ by 45 μ in fæces in large numbers* yolk cells tightly packed

Life history —Egg passed in water Operculum lifted ciliated hooked onchosphere or coracidium (22–30 μ) emerges resembles ball Swims by cilia dies in 24 hours Swallowed by freshwater crustacea (water fleas *Cyclops strenuus Diaptomus gracilis D oregonensis* U S A) hooks tear hole in intestinal wall (may kill Cyclops) *Outside gut becomes procercoid 50–60 μ with terminal spherical* appendix with six hooklets (as in onchosphere) then swallowed by *second intermediary* fish pike perch salmon trout grayling barbel in Africa pike wall eye burbot in U S A *Procercoid* penetrates stomach after 3–4 days in body cavity encysts as *plerocercoid* (or sparganum) 6 mm in muscular and connective tissues then eaten with roe (caviare) or insufficiently cooked fish and develops in 5–6 weeks into adult *Diphyllobothrium*

Clinical features —Symptoms usually trifling In small percentage produces severe anæmia (of pernicious type) Dried or alcoholic extract of worm causes destruction of r b c but not proportionally of hæmoglobin Anaemia caused by absorption of vitamin B_{12} by worm in intestine

Diagnosis —Usually easy by very numerous eggs in fæces

Treatment.—Worms easily expelled by *Filix mas* (p 237) tetra chlorethylene or oleoresin of aspidium

D minor claimed by Russians as separate species from L. Baikal Life history similar second intermediary different species of salmonidæ lavaret grayling etc

Diphyllobothrium mansoni

Adult in dog *plerocercoid* or *sparganum* in man dog wolf fox, cat, leopard tiger Japan China E Africa, Australia British Guiana Resembles *D latum* 6–10 m more delicate structure egg narrower and ellipsoid Plerocercoid (*Sparganum mansoni*) in man occasionally in kidneys iliac fossa pleural cavity urethra, subcutaneous tissues

Ocular sparganosis—In Tonquin Japan China worm in orbit pain redness œdema of eyelids lacrymation (Treatment by tarsorrhaphy) Under natural conditions in frog *Rana nigromaculata* or snake *Elaphe climacophora* probably contracted by man through Chinese practice of applying split frogs as poultices to sores on hands

Life history—As in *D latum* first intermediary *Cyclops leuckarti*

Spirometra mansonoides

May attain length of 1 m by 5 mm Adult in intestine of cat Life history probably similar to above Larval stage *Sparganum proliferum* In man plerocercoids in large numbers in walls of alimentary canal mesentery kidney lungs heart brain Japan Florida

Body of cyst contains calcareous corpuscles easily enucleated but prognosis grave owing to numbers

OTHER RARER TAPEWORMS

Raillietina celebensis *I madagascariensis* and *R quitensis* found rarely in Siam British Guiana Mauritius Formosa and Ecuador Numerous coalhammer hooklets on suckers and rostellum unilateral genital pores on proglottides Ripe segments contain egg capsules Ovoidal eggs possess large hooklets Usually parasites of birds and rats

Inermicapsifer arvicanthidis and *I cubensis* In Kenya Congo and Cuba Recently shown by Fain to be identical In Central Africa normally parasites of hyracoidea and rats Probably imported by African rodents to Cuba

2 **Cyclophyllidea.**—Round suckers genital orifice marginal

"PORK TAPEWORM" *Tænia solium*

Geographical distribution—Co-extensive with pig Unknown in Mahommedan and Jewish countries In upper third small intestine

Typical tapeworm 2–3 m (exceptionally 8 m) Head globular quadrangular 1 mm in diameter Rostrum short pigmented with double row of hooklets four projecting suckers Mature proglottides 12 mm by 6 mm each has *marginal* genital pore Uterus median with 7–10 *stout diverticula* Terminal segments in fæces show independent movement and migrate outside anus

Egg—31–56 μ round two radially striated shells contains six hooked onchosphere

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Ætiology —*D latum* long broad flat tapeworm grey translucent may attain 10 metres Coiled in small intestine Scolex 3 mm two slit like suckers thin neck 3–4 000 proglottides Genitalia complicated rosette shape twisting of uterus Dorsal aspect contains main male elements ventral female No segments passed in fæces

Egg —Brown operculated 70 μ by 45 μ in fæces in large numbers yolk cells tightly packed

Life history —Egg passed in water Operculum lifted ciliated hooked onchosphere or coracidium (22–30 μ) emerges resembles ball Swims by cilia dies in 24 hours Swallowed by freshwater crustacea (water fleas *Cyclops strenuus Diaptomus gracilis D oregonensis* U S A) hooks tear hole in intestinal wall (may kill Cyclops) Outside gut becomes *procercoid* 50–60 μ with terminal spherical appendix with six booklets (as in onchosphere) then swallowed by *second intermediary* fish pike perch salmon trout grayling barbel in Africa pike wall eye burbot in U S A Procercoid penetrates stomach after 3–4 days in body cavity encysts as *plerocercoid* (or sparganum) 6 mm in muscular and connective tissues then eaten with roe (caviare) or insufficiently cooked fish and develops in 5–6 weeks into adult *Diphyllobothrium*

Clinical features —Symptoms usually trifling In small percentage produces severe anæmia (of pernicious type) Dried or alcoholic extract of worm causes destruction of r b c but not proportionally of hæmoglobin Anaemia caused by absorption of vitamin B_{12} by worm in intestine

Diagnosis —Usually easy by very numerous eggs in fæces

Treatment —Worms easily expelled by *Filix mas* (p 237) tetra chlorethylene or oleoresin of aspidium

D minus claimed by Russians as separate species from L Baikal Life history similar second intermediary different species of salmonidæ lavaret grayling etc

Diphyllobothrium mansoni

Adult in dog *plerocercoid* or *sparganum* in man dog wolf fox cat leopard tiger Japan China E Africa Australia British Guiana Resembles *D latum* 6–10 m more delicate structure egg narrower and ellipsoid Plerocercoid (*Sparganum mansoni*) in man occasionally in kidneys iliac fossæ pleural cavity urethra subcutaneous tissues

Ocular sparganosis—In Tonquin Japan China worm in orbit pain redness œdema of eyelids lacrymation (Treatment by tarsorrhaphy) Under natural conditions in frog *Rana nigromaculata* or snake *Elaphe climacophora* probably contracted by man through Chinese practice of applying split frogs as poultices to sores on hands

Life history—As in *D latum* first intermediary *Cyclops leuckarti*

Spirometra mansonioides

May attain length of 1 m by 5 mm Adult in intestine of cat Life history probably similar to above Larval stage *Sparganum proliferum* In man plerocercoids in large numbers in walls of alimentary canal mesentery kidney lungs heart brain Japan Florida

Body of cyst contains calcareous corpuscles easily enucleated but prognosis grave owing to numbers

OTHER RARER TAPEWORMS

Raillietina celebensis R mada ascarensis and *R quitensis* found rarely in Siam British Guiana Mauritius Formosa and Ecuador Numerous coalhammer hooklets on suckers and rostellum unilateral genital pores on proglottides Ripe segments contain egg capsules Ovoidal eggs possess large hooklets Usually parasites of birds and rats

Inermicapsifer arvicanthidis and *I cubensis* In Kenya Congo and Cuba Recently shown by Fain to be identical In Central Africa normally parasites of hyracoidea and rats Probably imported by African rodents to Cuba

2 **Cyclophyllidea**—Round suckers genital orifice marginal

"PORK TAPEWORM" *Tænia solium*

Geographical distribution—Co-extensive with pig Unknown in Mahommedan and Jewish countries In upper third small intestine
Typical tapeworm 2–3 m (exceptionally 8 m) Head globular quadrangular 1 mm in diameter Rostrum short pigmented with double row of hooklets four projecting suckers Mature proglottides 12 mm by 6 mm each has *marginal* genital pore Uterus median with 7–10 *stout diverticula* Terminal segments in fæces show independent movement and migrate outside anus

Egg—31–56 μ round two radially striated shells contains six hooked onchosphere

Life history —Mature segments in fæces pass out and are eaten by pig Man occasionally infected (cysticercosis) Onchosphere penetrates gut and enters blood then in muscles loses hooks and becomes *Cysticercus cellulosæ* Pork infected is measly pork

In alimentary canal bladder is absorbed by gastric juice Head evaginated passes *to small intestine* where scolex fixes itself to gut wall and forms proglottides

Clinical features —Usually no symptoms In debilitated and in children may cause gastro intestinal disturbance possibly anæmia

Treatment —See p 237

CYSTICERCOSIS

Accidental ingestion of eggs of *T solium* man serves as intermediary host Onchospheres migrate to muscles of tongue neck ribs lungs liver heart and eye and more especially brain

Geographical distribution —Cysticercosis has been reported from nearly every country including England Most extensive infections in British soldiers especially from India

Pathology —Cysticercus in brain surrounded by neuroglia lymphocytes and few plasma cells when dead and degenerated acts as irritant focal necrosis around cyst Then becomes calcified commencing in scolex cyst capsule unaffected Process may occupy three years or longer

Clinical features —Occasionally associated with intestinal infection of *T solium* Jacksonian epileptic fits with cerebral cysticercosis cyanosis biting of tongue incontinence sometimes fatal may suggest cerebral tumour Mental degeneration loss of memory and higher senses

In muscles cysticerci cause no general reaction gradual development of small subcutaneous intramuscular *swellings Sometimes* toxæmia and pyrexia Often cysticercosis diagnosed accidentally *by X ray*

Diagnosis —Palpable cysts in tissues size of pea and even larger up to pigeon s egg *Excise and cut section to show structure of* cysticercus translucent membrane with central milk spot *Nodules usually appear in crops sometimes* difficult to find

X ray examination no use unless cysts are calcified Then elongated shadows fully calcified cyst has characteristic appearance Eosinophilia not marked no aid to diagnosis Complement fixation tests inconclusive

Precipitin test with antigen from *Cysticercus cellulosæ* sometimes employed Intradermal Casoni test (p 240) *positive in 50 per cent* No constant change in C S F sometimes excess of lymphocytes and eosinophiles colloidal benzoin reaction sometimes positive

Treatment —Rarely successful Localization of cysticerci in brain by radiography and removal Intravenous injections of antimony tartrate useless Luminal and bromides *helpful in controlling fits* If *T solium* is present in intestine *Filix mas* is indicated

Prophylaxis —Regurgitation of proglottides of *T solium* into stomach suggested probably from eating sausages made from pigs intestines or food contaminated by pig excreta Control of sausage meat indicated Fæces disposal Fly control eggs carried by flies from infected fæces

' BEEF TAPEWORM ' *Tænia saginata*

Geographical distribution —World wide wherever beef is eaten especially in Abyssinia multiple infections common Worm found coiled up in small intestine

Ætiology —*T saginata* differs from *T solium* in several points especially absence of rostellum and hooks Semi transparent 4–10 m 2 000 segments sometimes *scolex* pear shaped 1–2 mm pigmented with four lateral suckers and sucker like organ at apex Genital pore marginal at hinder end of proglottis alternating between right and left margins 20–35 lateral branches on each side of uterus

Egg —30–40 μ by 20–30 μ indistinguishable from those of *T solium*

Life history —Gravid proglottides in fæces creep into grass and disintegrate Eggs eaten by ox Onchospheres set free pass into small intestine bore through wall and are carried to muscles especially pterygoids diaphragm tongue

Cysticerci —7 5–9 mm by 5 5 mm live 8 months in ox measly beef eaten by man bladder digested liberated scolex passes to small intestine and affixes itself by suckers to gut wall

Clinical features —May occasionally cause abdominal pain and some anæmia.

Treatment of tapeworm infections —

Filix mas —Preliminary starvation two days tea toast fluids + glucose D Extract of filix mas 45–90 min (2 8–5 6 c c) in gelatin capsules For adult man 126 min for female 90 min

No Breakfast—cup of tea at 7 a m
8 a m 2 capsules of 15 min *Filix mas*
8 30 a m repeat
9 a m repeat
Complete quiet sips of water
9 30 a m *Ol terebinth* 20 min (0 124 c c) emulsified with gum acacia
10 30 a m Sodi sulph ½ oz (14 7 c c)

Directly purging commences give hot water enema of 1½ pints (assists in dislodging worm and separating head) All stools strained and examined for head *N B* —If head is not found useless to give further course of treatment till segments again appear in stools

Atebrin (mepacrine) lethal to tapeworms in doses of 0 9–1 gm dislodges head of worm Best given in combination with *Filix*

middle of the proglottis The number of testes is 21–29 and they lie behind the posterior end The uterus has no lateral branches The length of the mature worm is 1 4–3 4 mm in *E granulosus* it is 5–8 mm

Clinical features —Dogs infected by eating offal especially of sheep Man by close association with dog Symptoms vary according to *site of cyst toxæmia pyrexia urticaria In brain cerebral* tumour In liver spleen peritoneum simulates malignant growths In lung compression fluid in pleural cavity In kidney resembles hydronephrosis Local symptoms in long bones *heart orbital cavity*

Cyst wall outer chitinous inner germinal with muscular fibres calcareous bodies and glycogen Bladder watery fluid sp g 1007 albumin and protein allied to casein Intracystic toxin hydatid fluid in abdominal cavity produces anaphylactic reaction and shock

Diagnosis —Cystic swelling giving hydatid thrill on puncture yielding hooks and scoleces Precipitin reaction equal parts of hydatid fluid and serum in incubator precipitate forms Complement fixation (Wassermann technique) antigen (0 4 c c) from scoleces macerated with alcohol

Intradermal test (Casoni) hydatid fluid of sheep or man injected intradermally reaction in 10 minutes large wheal surrounded by erythema Secondary reaction 8 hours later

Treatment —Surgical In man cysts tend to die and become calcified Rarely suppurate

Cænurus cerebralis —Larval form of *Tænia multiceps* of sheep adult in intestine of dog rare in man Causes symptoms of cerebral tumour *C glomeratus* normally in gerbille found in abscess of chest wall in Nigeria

A LIST OF DRUGS EMPLOYED IN THE TREATMENT OF TROPICAL DISEASES

Acidum ascorbicum *Vitamin C Cevitamic Acid Redoxon Proscabin*
Enolic form of 3 *keto-1 gulofuranolactone*
Scurvy wound healing
Oral tab *acidi ascorbici* 50 mg (0 7 gr) three times daily
In acute cases intravenous

Acranil *Hydrochloride of acridine*
Giardiasis (Lambliasis) Balantidiasis
Oral tab 0 5 gm (7 7 gr) Three tablets daily for five days
No toxic effects

Alepol. *Sodium hydnocarpate or sodium gynocardate*
Leprosy
Subcutaneous intramuscular or intravenous 1–10 cc of 1 or 2% solution.

Anabin. *Kurchi-bismuth-iodide*
Alkaloid of kurchi is *conessine*
Amœbiasis
Oral tab 0 25–0 65 gm. (3·7–10 gr)

Aneurin. *Aneurinæ Hydrochloricum B P Thiamine Hydrochloride Vitamin B_1*
3 (4 *Amino 2 methylpyrimidine 5) methyl 5 B hydroxyethyl thiazolium chloride hydrochloride*
Beriberi Burns Varicose Ulcers
Oral tab 3 mg Injection 25 mg (0 37 gr) in 1 c c Store protected from light

Anthical
Zinc oxide and anthisan
Lotion for sunburn and insect stings

Anthiomaline *Lithium antimony thiomalate*
Schistosomiasis Lymphogranuloma inguinale Leishmaniasis Filariasis (*W bancrofti*)
Intramuscular 0 5–4 c c. (1 c c. = 10 mg Sb)
10–20 injections 2–3 per week.

Anthiphen. (M & B) *Dichlorophen*
2 2-*dihydroxy 5 5-dichloro-diphenyl methane*
Tæniasis *Tænia saginata*
Oral tab 0 5 gm per 7 25 kg in one dose at 10 a m
Total dosage 6 gm (92 5 gr) in three equal amounts at intervals of 8 or 12 hours

Anthisan.
Antihistamic for allergic conditions in filariasis and schistosomiasis
Oral tab 0 3 gm (4 6 gr) increasing to 1 gm (15 4 gr) daily in divided doses with food.

Antimonii et Potassi Tartras B P *Tartar Emetic*
Kala azar, Oriental sore Espundia Yaws Lymphogranuloma inguinale Ulcerating Granuloma Trypanosomiasis Relapsing Fevers Lepra reactions Schistosomiasis
Intravenous in solution in distilled water 0 03–0 12 gm (0 46–1 8 gr) Alternate days—up to total of 2 5 gm (38 5 gr)

Antimonyl a a dimercapto potassium succinate (*T W S.B*) (Friedheim)
Soluble in water—30%
Schistosomiasis (*S mansoni*) in Brazil
Intramuscular injection 0 5 gm Total 32 gm for 13 days 23–42 mg per kg
Intravenous 0 7–2 3 gm total (10 8–35 gr)

Antimosan. *Von Heyden* 661
Potassium antimonyl pyrocatechol sulphonate Contains 12 5% antimony in trivalent form
Kala azar and other forms of Leishmaniasis
Intravenous or intramuscular 0 2 gm (3 gr) twice weekly

Antrenyl (Ciba)
2 diethylaminoethyl a cyclohexyl a phenylglycollate methobromide
Antispasmodic for relief of gastro intestinal pains
Oral tab 5–10 mg (0 07–0 15 gr) four times daily

Antrycide chloride
4-amino 6 (2 amino 6 methylpyrimidyl 4 amino) quinaldine 1 1 -dimetho chloride
Trypanosomiasis of cattle and man
Injection single dose of 1 mg per kg for *Trypanosoma congolense T rhodesiense T brucei T evansi T equiperdum* and *T equinum*

Antrypol B P *Suramin Bayer 205 Germanin Fourneau 309 Moranyl Naganol Naphuride*
Urea of acid dimeta aminobenzoyl meta aminoethyl ben oyl l-naphthyl-amino 4 6 8 trisulphonate of soda
Trypanosomiasis (*T gambiense* and *T rhodesiense*) Onchocerciasis
Intravenous or rarely intramuscular 1–3 gm (15 4–46 2 gr) Active in early stages of trypanosomiasis

Aralis (Winthrop)
Tablets containing 75 mg of Aralen (chloroquine diphosphate) and 250 mg of Milibis (bismuth glycolylarsanilate)
The quantities are chosen to give a balanced therapeutic action in both prophylactic and therapeutic treatment of amœbiasis
Intestinal and extra intestinal amœbiasi
Dose Tab 6 daily for 7 days
Prophylactic 3 tablets daily on 2 days a week

Areca B P C. *Betel Nut*
Dried ripe seeds of Areca catechu *Contains not less than 25% of arecoline*
Tæniasis
Oral powder or emulsion 1–4 gm (15–60 gr) Effective in combination with oleoresin of aspidium
Given as enema 1 20

Arsenamide *Sodium Thiacetamide*

p-p(bis-carboxy methyl mercapto) arseno benzamide

Filariasis—*W bancrofti* and *W bancrofti* var *pacifica*

Intravenous or intramuscular injection in 2 / solution 1 mg per kg daily for 15 days Average daily dose 0 5 gm (7 7 gr) Total 7 5 gm (185 gr)

Arsthinol (Balarsen) *S T B*

N 2-acetylamino-4 methylol cyclo (ethylene dimercaptoarseno) phenol

Amœbiasis Yaws

Oral tab 10 mg (0 15 gr) daily for 5 days

Ascabiol. *Benzevan Proscabin*

Benzyl benzoate

Scabies Pediculosis (*P capitis* and *P pubis*)

Local application.

Auremetine

Combination of periodides of *emetine* and *auramine* containing 28 / emetine 16 auramine and 56 / iodine

Amœbiasis in chronic stage

Oral in emplets (enteric-coated tablets) or slipules 0 12–0 2 gm. (1 8–3 gr) Total 4 gm. (61 7 gr)

Aureomycin. *Chlortetracycline*

Antibiotic from *Streptomyces aureofaciens*

Undulant fevers Typhus Q fever Lymphogranuloma venereum Psittacosis Amœbiasis Yaws Coccidiomycosis

60 mg per kg in capsules of 250 mg (3 7 gr) four times daily for 5 days Important that each capsule should be taken with a cup of milk or water Intravenous or intramuscular 3 mg per kg

Avomine.

8-chloro theophyllinate of bromethazine

Nausea Travel Sickness Cholera.

Oral tab 25 mg (0 37 gr)

Azacrin. *Amino-aza-acridine*

2 methoxy 6-chloro 9 (5 diethyl amino 2-pentyl)-amino 3-aza acridine hydrochloride

Malaria Giardiasis

Oral tab 0 4 gm. (6 1 gr) for 5 days.

B 15

(*2 Hydroxy 5-arsonophenyl methane*)

Amœbiasis and Amœbic Hepatitis

Oral 15–65 gm (231 1 003 gr) over a period of 10 30 days.

Recommended dosage 2 gm (30 8 gr) daily

Bacitracin.

Antibiotic from strains of *Bacillus subtilis*

Amœbiasis.

Oral, tab 80 000 units for 10 days Intramuscular, 50 000 units for 7 days Intravenous contra indicated. Bacitracin is nephrotoxic.

9

Bal (Dimercaprol) *British Antilewisite*
Inhibits metal containing compounds
Ampoules containing 100 mg Intramuscular injections—100 1 (1 5 gr) at 4 hourly intervals 2nd 3rd and 4th days 100 mg tw 5th and 6th days 100 mg daily

Berberine sulphate (India only) *Orisol*
Oriental sore
Subcutaneous injection or as ointment *0 06–0 3 gm (0 9–4 6 gr)*

Betanaphthol B P
B-naphthol
Ancylostomiasis Ascariasis Tæniasis
Oral 0 2–0 65 gm (3–9 9 gr)

Bismosol
10% solution of potassium sodium bismutholartrate (containing 0 3 piperazine) in glucose solution
Syphilis Yaws
Intramuscular 0 1 c c

Bismuth oxychloride
Yaws
Lupus erythematosus (in 10% ointment)
Oral 0 6–2 gm (9 2–30 8 gr)

Bromoguanidine
Analogue of paludrine in which a bromide atom replaces chlorine
Possesses antimalarial properties corresponding to those of paludrine

Camoform *Biallylamicol, S N 6771 P A A 701*
6 6 diallyl a a bis (diethylamino) 4 4 bi o cresol
Allied to camoquine
Amœbiasis
Oral tab 2 gm (30 8 gr) daily for 10–14 days

Camoquine *Amodiaquine S N 10751 Flavoquine Miaquin CAM AQ*
7 chloro 4(3 diethyl aminomethyl 4 hydroxyanilino) quinoline
Malaria Giardiasis
Oral, tab 0 2 gm (3 gr) of base as dihydrochloride
Adults 0 6 gm (9 2 gr) children 0 4 gm (6 1 gr)
(Each 261 mg tablet of camoquine contains 200 mg of base)

Carbarsoneum B P
Amibiarson Leucarsone Amabevan
4 carbaminophenylarsonic acid
Yaws Chronic amœbiasis
Oral tab 0 25 gm (3·7 gr) or by rectum in solution 2 gm (30 8 gr dissolved in 200 c c 2% sodium bicarbonate solution as retention enema

Carbonei Tetrachloridum B P *Tetrachlormethane Tetraform CCl_4*
Effective anthelmintic for Ascaris Ancylostoma and Tapeworms
Now largely replaced by Tetrachlorethylene
Oral in gelatin capsules 3 c c (48 6 min) maximum dosage

Chaulmoogra oil

Oil expressed from seeds of *Hydnocarpus kurzii*

Leprosy
Oral intradermal subcutaneous or intramuscular 0 3–5 c c

Chenopodium oil *Oil of American Wormseed*

Oil distilled with steam from fresh flowering and fruiting plants of Chenopodium ambrosioides var anthelminticum Contains 65% W/W of ascaridole

Ascariasis Ancylostomiasis *Larva migrans*
Oral in capsules or in mixture 0 2–1 c.c.

Chiniofon B P *Quinoxyl Yatren Anayodin Dysentulin.*

Sodium 7 iodo-8 hydroxy-quinoline 5 sulphonate

Amœbiasis Bacillary Dysentery
Oral, tab 0 06–0 5 gm (0 9–7 1 gr) Retention enemata 2½–3% solution 1–5 gm (15 4–77 1 gr)

Chloromycetin *Chloramphenicol* B P Add

Antibiotic originally isolated from *Streptomyces venezuelæ* Now synthetic. *D ( ) threo 2 Dichloroacetamido 1 p nitrophenyl 1 3 propanediol*

Typhus fevers especially Mite typhus and Typhoid Bartonellosis Whooping cough Gonorrhœa.
Intramuscular or intravenou injections 1–5 gm (15 4–77 1 gr) daily
Oral, capsules 750 mg four times daily for 6 days May produce aplastic anæmia agranulocytosis and thrombocytogenic purpura
Chloromycetin palmitate suspension (P D & Co) Bitterless derivative for treatment of infants and children

Chloroquine *Aralen Resochin Avlochlor* (I C I)

7-chloro 4(4 diethyl amino 1 methyl butyl amino) quinoline diphosphate

Malaria (powerful schizonticide) Hepatic Amœbiasis Balantidiasis Giardiasi *Hymenolepis nana Trichuris trichiura*
Oral Suppressive for malaria 0 3 gm weekly Injection ampoules of 5 c.c (equivalent to 40 mg (0 6 gr) of base per c.c) Curative First day 3 doses of 0 3 gm followed by one dose of 0 3 gm daily for 3 days Dosage in terms of base Side effects pruritis of hands bleaching of hair

Cinchona B P C. *Cinchona Febrifuge*

Contains mixed cinchona alkaloids in varying proportions
Malaria
Oral tab 0 06–0 6 gm (0 9–9 2 gr) two or three times daily
Used as a substitute for quinine

Compound 6257 (Ciba) India

Condensation product of sulphathiazole and formaldehyde

Cholera
Oral 6 gm (92 5 gr) Total dosage 28 gm (432 gr) recommended

Conteben *Thiacetazonum Thiosemicarbazone*
(4-acetylamino benzaldehyde thiosemicarbazone)
Leprosy
Oral Powder 12 5 mg (1 8 gr) to 250 mg (3 7 gr)
Maximum 400 mg (6 1 gr)
Course of 1 year

Cortisone ointment
Seborrhœa Allergic reactions due to fungus infections of feet (athlete s foot)

Crystal Violet B P
Gentian violet Methyl rosaniline Hexamethyl pararosaniline hydrochloride
Oxyuriasis clonorchiasis *Hymenolepis nana*
Oral tab 0 5 gm (7.7 1 gr) t d s for 7 days for oxyuris *18 mg per* kg 10–20 days for clonorchiasis—total 1 2 gm (18 4 gr)

Dapsonum B P C. Supp *D D S Avlosulphon D.A D P.S*
4 4 *Diamino diphenyl sulphone*
Leprosy Mycetoma Dermatitis herpetiformis
Oral, tab 100 mg (1 5 gr) twice weekly

Daraprim *Pyrimethamine Malocide*
5 (p chlorophenyl) 2 4 diamino 6 ethylpyrimidine
Malaria especially benign tertian.
Oral 10–20 mg (0 15–3 gr) or more daily 5 mg (0 7 gr) daily suppressant

D B P *Dibutylisphthalate B P C Butylphthalate*
Insect repellent and more effective than D M P against trombidid mites
Impregnation of clothing 1 oz to set of clothing (= 30 c.c)

Diasone. *Promanide Sulphoxone sodium*
Derivative of Dapsone.
4 4 *Diamino diphenyl sulphone disodium formaldehyde sulphoxylate*
Leprosy Tuberculosis
Oral tab Maximum dose 100 mg (1 5 gr) daily for 2 weeks
Intravenous in severe cases

Dibistin (Ciba)
Sugar coated tablets containing 0 05 gm (0 7 gr) antistin and 0·025 gm. (0 37 gr) pyribenzamine
A cream is also made for local application.
Has a double antihistamine effect in seasonal allergic conditions solar dermatitis pruritic dermatitis hay fever etc

Dicophanum B P Add *DDT*
1 1 1 trichloro 2 2 di-p chlorophenylethane
Chronic poisoning arises from inhalation of dust or absorption through the skin. Causes loss of appetite muscular weakness and fine tremors
Insecticide and larvicide Effective against head and body lice and typhus epidemics have been aborted by blowing mixture of 2–10% dicophane and talc between skin and clothing as dust or as oily spray for mosquito control Residual sprays of walls with 5% solution in paraffin oil. 10 c c. per sq yard effective for 4 months For quick knock down pyrethrum is added to dicophane spray solutions

Di iodohydroxyquinoline B P

Diodoquin Dihaloquin Sacorquin Embequin
Compound of quinoxyl with 63·9% iodine

Chronic amœbiasis.
Oral, tab 0 25–0 3 gm (3 7–4 6 gr) 3–10 daily for eradication of *E histolytica cysts*

Diphenan B P *Butolan Oxylan*

p-benzylphenyl carbamate
Oxyuriasis
Oral 0 5 gm (7 7 gr) three times daily

Diphetarsone *Bimarsal*

Intestinal amœbiasis and when combined with chloroquine diphosphate has given satisfactory results in malaria
Oral tab Bemarsal 2 gm (30 8 gr) with chloroquine 0 3 gm (4 6 gr for 10 days

Dithranol B.P *Anthralin Cignolin Derobin*

1 8-*dihydroxyanthranol*
Oriental Sore, Ringworm skin affections
As an ointment 0 25–3%

D.M.P Dimethylphthalas B P C.

Repellent for insects mosquitoes tick fleas and especially *Trombicula akamushi* and other mite vectors of scrub typhus
Clothing impregnated but should not be used on artificial silks
D M P cream containing 35% D I M P repellent

Emetine and Bismuth Iodide B.P E B I

Bismuth iodide of emetine
Amœbiasis
Oral, 0·02–0 12 gm (0 3–1 8 gr) Total 1 5–2 gm (23 1–30 8 gr) In gelatin capsules (slipules) emplets enteric coated tablets no recommended

Emetine Hydrochloride B P

Emetine is alkaloid of ipecacuanha
Amœbiasis Liver Abscess Oriental Sore Clonarchiasis Paragonimiasis
Injection deep subcutaneous or intramuscular
0·06 gm (1 gr) usually in daily doses
Total 6–12 gr (0 38–0 77 gm) Powerful effect in acute Amœbic Dysentery and in Amœbic Hepatitis

Entacyl (B D H)

Piperazine adipate
Ascaris lumbricoides Trichuris trichiura Oxyuris vermicularis (thread worm)
Oral tab 300 mg (4 6 gr) 2 tab three times daily One tablet for each year of life Children over six same dose as adults For oxyuris continue for 7 days
In syrup form for children

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(4 acetylamino benzaldehyde thiosemicarbazone)
Leprosy
Oral Powder 12 5 mg (1 8 gr) to 250 mg (3 7 gr)
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Diphetarsone *Bimarsal*

Intestinal amoebiasis and when combined with chloroquine diphosphate, has given satisfactory results in malaria
Oral tab Bemarsal, 2 gm (30 8 gr) with chloroquine 0 3 gm. (4 6 gr) for 10 days

Dithranol B P *Anthralin Cignolin Derobin*

1 8-dihydroxyanthranol

Oriental Sore Ringworm skin affections
As an ointment 0 25–3 /

D.M P Dimethylphthalas B P C.

Repellent for insects mosquitoes tick fleas and especially *Trombicula akamushi* and other mite vectors of scrub typhus

Clothing impregnated but should not be used on artificial silks
D M I cream containing 35 / D I M P repellent

Emetine and Bismuth Iodide B P E B I

Bismuth iodide of emetine

Amoebiasis
Oral 0·02–0 12 gm (0 3–1 8 gr) Total 1 5–2 gm (23 1–30 8 gr) In gelatin capsules (slipules) emplets enteric coated tablets not recommended

Emetine Hydrochloride B P

Emetine is alkaloid of ipecacuanha

Amoebiasis Liver Abscess Oriental Sore Clonarchiasis Paragonimiasis
Injection deep subcutaneous or intramuscular
0·06 gm (1 gr) usually in daily doses
Total 6–12 gr (0 38–0 77 gm) Powerful effect in acute Amoebic Dysentery and in Amoebic Hepatitis

Entacyl (B D H)

Piperazine adipate

Ascaris lumbricoides Trichuris trichiura Oxyuris vermicularis (thread worm)
Oral tab 300 mg (4 6 gr) 2 tab three times daily One tablet for each year of life Children over six same dose as adults For oxyuris continue for 7 days
In syrup form for children

Entamide R.D 3803
Dichloracet 4 hydroxy N methylanilide
Amœbiasis
Oral tab 12 mg per kg for 10 days

Enterovioform (Ciba)
Iodochlorohydroxyquinoline with sapamine
Infantile summer diarrhœa colitis and Amœbic Dysentery
Oral capsules 0 75 to 1 gm (11 5–15 4 gr) in divided doses of 0 25 gm for 10 days

Erythromycin *Ilotycin Erythrocin Erythromycin stearate*
Antibiotic from Streptomyces erythreus
Amœbiasis Toxoplasmosis
Oral capsules Dosage 300 mg four times daily

Etharsanol.
Sodium 4 β hydroxyethylaminophenylarsonate
Trypanosomiasis (*T gambiense*)
Intravenous 2 gm (30 gr)

Ethyl Esters of Hydnocarpus Oil B P *Antileprol Chaulmestrol Moogrol*
A mixture of the ethyl esters of the unsaturated fatty acids (chiefly chaulmoogric and hydnocarpic acids) of hydnocarpus oil
Leprosy
Intradermal subcutaneous or intramuscular 2–5 c c (32 4 min or 1 35 3)

Folic acid. *Pteroylglutamic acid*
Synthetic product resembling *Lactobacillus casei* factor of liver and yeast
Produces hæmopoietic response in macrocytic anæmia.
Tropical sprue Nutritional Tropical Macrocytic Anæmia
Oral tab 5–30 mg (0 07–0 46 gr)
Folvite = Sodium salt for parenteral administration 15 mg per c c. used in conjunction with liver extract for Pernicious Anæmia

Fourneau 710
Plasmocide Rhodoquine
6 methoxy-a-diethylamino n-prophylaminoquinolene
Malaria.
Oral tab 0 02–0 04 gm (0 3–0 6 gr) for 7 days

Fumagillin *Fumidil*
Antibiotic isolated from Aspergillus fumigatus
Amœbic Dysentery Active on cultures of *E histolytica* 1 10 million
Oral capsules containing 10 mg (0 15 gr) Dose is 30–60 mg (0 46–0 9 gr) daily in divided doses for 10 days

Gammabenzene *Benzene hydrochloride Lindane Gammexane Lorexane*
Application for nits active against mosquitoes flies lice and ticks
Lotion contains gamma benzene Hcl gr 1 (0 06 gm) emulsifying wax gr 35 (2 26 gm.) xylene of commerce min. 144 (8·9 gm.) lavender oil, min 10 (0 6 gm.) water ad. fl oz. 2 (60 c.c.)
Rub into hair and roots Do not wash head for one day
Benzene hexachloride ointment 1% Active and rapid cure for scabies

Glaucarubin. (Merck Sharp and Dohme)

Derived from Simaruba glauca
a-methyl-a hydroxy butyric acid combined with hexahydroxylactone

Amoebiasis
Oral tab 1 mg per kg for 10 days

Guanimycin.

Mixture of Streptomycin and Sulphaguanidine Streptomycin 5 gm Sulphaguanidine 3 gm (46 2 gr) per fluid ounce in suspending agent Add 1½ fl oz (45 c.c) of cold water and shake

Bacillary dysenteries
Suspension Oral Two tablespoonfuls every four hours—children one tablespoonful every three hours

Hetrazan (844) *Banocide Notezine Diethylcarbamazine B P C Supp Diaethylcarbamazine Citras Acidus*

1-diethylcarbamyl 4 methyl piperazine hydrochloride and hetrazan and hydrogen-citrate (Banocide)

Filariasis (*W bancrofti W bancrofti* var *pacifica W malayi*) *Loa loa Onchocerca volvulus Mansonella ozzardi Dipetalonema perstans* Larva migrans *Ascaris lumbricoides* Tropical Eosinophilia
Oral tab 0 5–2 mg per kg three times daily 100–300 mg (1 5–4 6 gr) for average adult

Hexamine B P C. *Aminoform*

Hexamethylene tetramine

Urinary infections (*Bact coli*) Cholecystitis
Oral tab 0·6–2 gm (9 2–30 8 gr)

Hexylresorcinol B P C. *Caprokol*

1 3-dihydroxy 4 hexylbenzene

Ascaris lumbricoides Ancylostoma duodenale Trichuris trichiura
Oral cachets or pills 0·2 gm (3 gr) 5 daily
Also 1 2 000 solution rectal enema for oxyuriasis

Holarrhena B P *Kurchi Coorchi*

Contains the alkaloids conessine holarrhenine kurchicine and kurchine

Amoebiasis
Oral, 0·25–0·6 gm (3·7–9·2 gr) Preparation used in India

Hydnocarpus Oil B P

Fatty oil obtained by cold expression from seeds of *Hydnocarpus wightiana*

Leprosy
Injection intradermal subcutaneous or intramuscular 2–5 c c (32 4 min – 1 353)

Hydroxystilbamidine isethionate

2 hydroxy 4 4-diamidinostilbene di (B hydroxyethanesulphonate)

Kala azar particularly antimony resistant cases Blastomycosis, *Candida albicans* infections and other systemic fungal infections Palliative for myelomatosis
Intravenous, 3–5 mg per kg Adult dose 250 mg in 10 c.c water injected slowly daily or on alternate days

Injectio Bismuth B P *Bisglucol Bismostab*

20% W/V precipitated bismuth, 0 5% V/V cresol in isotonic dextrose solution.

Yaws Syphilis
Injection intramuscular or deep subcutaneous 0 5–1 c c (8 1–16 2 min)

Injection of Bismuth Salicylate B P C. *Bisantol Bismosan*

10% suspension of bismuth salicylate in neutral vegetable oil

Yaws Syphilis
Oral tab 0 6–2 gm (9 2–30 8 gr)
Injection deep intramuscular or deep subcutaneous 2 c c. (32 4 min.) 60–200 mg (1 c.c. = 0 051 Bi) 0 9–3 min

Isoniazid *Isonicotinic acid hydrazide Nicetal Nydrazid I.N.H (International Symbol)*

Derivative of *iso nicotinic acid*

Leprosy Tuberculosis
In combination with dapsone
Oral tab 6–8 mg per kg Tab and capsules 50 mg (0 77 gr)

Kaolin Leve B P *Light kaolin Bolus alba, China clay*

Cholera
Oral suspension 200 gm (3086 gr) in 400 c c (15 5 oz) of water
Mist Kaolini et Morphinæ Light kaolin 30 gr (2 gm) sodi bicarb 10 gr (0 64 gm) tinct chloroformi et morphinæ 10 min (0 6 c c) water to ½ oz (15 c.c)

Kikuth's Sdt 386B

Arseno stibio compound of the salvarsan type

Bartonellosis
Intravenous 0 2 gm (3 gr)

Kousso *Cusso*

Dried female flowers of Brayera anthelmintica Kusotoxin active principle

Tæniasis *T saginata* in Abyssinia
Oral powder 1–4 gm (15–60 gr) in divided doses at half hour intervals Total dosage 8 gm. (123 4 gr) followed by purgative Effective if freshly prepared

Lacquin (Cow and Gate Ltd)

Milk powder containing quinine ethyl carbonate 2½ gr (0 16 gm) to tea spoonful

Malaria
Tasteless and suitable for children

Magnamycin *Carbomycin*

Antibiotic derived from *Streptomyces halstedi* Possesses amœbicidal action *in vitro*

Amœbiasis Toxoplasmosis
Oral, capsules 1–2 gm (15 4–30 8 gr) daily for 6–10 days
Dosis therapeutica 40–50 mg per kg

Male Fern B P *Filix Mas*

Ether ext act of dried rhizome and leaf bases of Dyopteris filix mas containing 25 % w/w filicin

Cestodiasis *Taenia Saginata T solium* and *Diphyllobothrium latum*
Oral liquid 3–5 5 c c. (48 6 mins –1 4 3) in syrup or in gelatin capsules each containing 15 min. followed by saline aperient.

Mandelic Acid B P C.

a hydroxy phenylacetic acid phenylglycolic acid
Urinary infections especially *Bact coli*
Oral, in syrup 2–4 gm (30–60 gr)

Melarsen oxide/BAL. *Melarsen B Arsobal* (France and Portugal)

p-(2 4-diamino 1 3 5 triazinyl 6)-aminophenyl arseno-γ B-dithiopropanol
A trivalent arsenical compound
Trypanosomiasis especially for advanced cases due to *T gambiense* and *T rhodesiense*
Intravenous 1 8–3 6 mg per kg Adult dose 2 5—5 c c. (40 5 mins.–1 35 3) of 3 6 % in propylene glycol daily for 3–4 days.
Second similar course one week later

Melarsen sodium

Monosodium salt of p (2 4-diamino 1 3 5-triazinyl 6)-aminophenyl arsonic acid
A pentavalent arsenical compound
Trypanosomiasis due to *T gambiense* especially for late relapsing tryparsamide resistant cases
Intravenous Freshly prepared 10 solution
Adults 1 gm (15 4 gr) adolescents 0 7 gm (10 8 gr) Children under 12 0 4 gm (6 1 gr) 8–12 injections at intervals of 5–7 days

Mepacrine Hydrochloride B P *Atebrin Quinacrine*

2-chloro 5(ω-diethylamino-α methylbutylamino) 7 methoxyacridine dihydrochloride
Malaria especially *P falciparum* Oriental Sore Giardiasis Cestodiasis *T saginata T solium D latum* Lupus erythematosus
Oral tab 0 05–1 gm (7 7–15 4 gr) maximum loading dose 0 3 gm. (4 6 gr) maximum daily dose for tapeworm 0 9 gm (13 8 gr)

Mepacrine Methane Sulphonate B P *Atebrin musonate*

Dimethanesulphonate of mepacrine
Malaria especially *P falciparum* Giardiasis
Intramuscular or subcutaneous Ampoules containing 0 12 and 0 36 gm
Doses vary from 0 05 to 0 1 gm (0 7–1 54 gr)

Mesulphen B P C. *Mitigal Sudermo (contains 25% of sulphur)*

2 6 dimethylthianthrene
Scabies Fungous infections of feet
Local application of standard solution

Milibis *Win Wintadon Bismuth glycolylarsinalate*

Bismuth derivative of oxy para N glycolyl arsanilate Contains 15 01% arsenic 41 81% bismuth

Chronic Amoebic Dysentery

Oral tab 0 25 gm (3 7 gr) three times daily 7–16 days

Miracil D Leucanthone hydrochloride B P C *Nilodin*

Hydrochloride of 1 methyl 4 beta diethyl-aminoethyl, aminothioxanthone

Schistosomiasis especially *S hæmatobium*

Oral tab 500 mg (7 7 gr) at twelve hour intervals up to 14 days. Usual dose for adult is 1 gm (15 5 4 gr) (7mg per kg.)

Blood concentration should be 300 mg %

Mycil (B D H)

Mycil ointment dusting powder contains fungicide chlorophenesin

Mycil pessaries contain chlorophenesin and D M 238 (hydroxy dichloro diphenyl methane)

Fungicidal preparation

Fungous infection of feet *Tinea circinata T cruris T unguium*

Mycostatin *Nystatin*

Antibiotic originally named fungicidin

Coccidioidomycosis

Has been shown to be fungistatic to cultures of *Coccidioides immitis*

Myocrisin *Sodium aurothiomalate*

Relapsing Fevers Lymphogranuloma inguinale Clonorchiasis.

Injection deep subcutaneous or intramuscular

0 01–0 05 gm. (0 15–0 7 gr) continued with 0 1 gm (1 5 gr) at weekly intervals.

Neoarsphenamine B.P

Neosalvarsan Novarsenobenzol

Sodium 3 3 diamino 4 4 dihydroxy arsenobenzene N methylene sulph oxylate

Relapsing Fevers (*S recurrentis S duttoni*)

Rat bite Fever (*S minus*), Yaws Syphilis Malaria Trypanosomiasis Tropical Eosinophilia

Intravenous 0 15–0 9 gm (2 3–13 8 gr)

Neocryl. *Sodium succinanilo-methylamide-p-arsonate*

Trypanosomiasis Syphilis

Intravenous 1 5 gm. (23 1 gr) at stated intervals

Neo hepatex

Proteolysed extract of liver for parenteral use Contains also Vitamin B_{12} in excess of 12 μmg per c c

Tropical Sprue Nutritional tropical megalocytic anæmia malarial anæmia.

Intramuscular, 2 c c. (32 4 mins) on alternate days

Neomycin.
Antibiotic obtained from *Bacillus fradiae*
Consists of three antibiotics known as neomycin complex
It is a good intestinal antiseptic and has been used successfully in the treatment of gram negative urinary tract infections. Neomycin contains a nephrotoxic factor

Neo premaline
An association of Chloroquine 0 15 gm (2 2 gr) Pamaquin 0·0075 gm (1·07 gr) and Rhodoquine 0·0075 gm (1·07 gr) the latter French preparation allied to pamaquin also called *Plasmocide* or Fourneau 710
Malaria.
Oral, one tablet three times daily for 10 days
Suppressive two tablets once a week

Neostam. *Stibamine glucoside* (B W & Co)
Nitrogen glucoside of sodium p-aminophenyl stibonate
Kala azar oriental sore Espundia
Intravenous 0 2 gm (3 2 gr) repeated at regulated intervals

Neostibosan *Von Heyden 693*
Diethylamino p-aminophenyl stibinate
Kala azar oriental sore Espundia.
Intravenous, or intramuscular 0 2 gm (3 gr) at frequent intervals up to total of 4 gm (61 6 gr)

Nicotamidum B P *Nicotinic acid amide*
Pyridine 3-carboxylic acid amide
Pellagra
Oral tablet 50–250 mg (0·77–3 85 gr) daily

Nicotinic Acid B P *Niacin*
Pyridine 3-carboxylic acid
Pellagra Ménière s syndrome
Oral tab 50–250 mg (0·77–3 85 gr) daily In serious cases also intravenous.

Nivaquine (M & B) is the trade name for Chloroquine sulphate Nivaquine (chloroquine sulphate) is known as Nivaquine B in U.S A. Nivaquine C is 3 *methyl 4 (diethylamino-pentyl) amino-7-chloroquinoline dihydrochloride* which also is active against all forms of malaria but is not procurable in Great Britain.

Nivembin (M & B)
Chloroquine-di iodohydroxy-quinoline tablets each containing chloroquine sulphate 65 mg and di-iodohydroxy-quinoline 300 mg
Amoebiasis and amoebic hepatitis
Oral tab. one three times daily

Novobiocin *Albamycin*
Antibiotic isolated from *Streptomyces niveus* or *actinomyces*
Identical with *cathomycin* and *cardelmycin* (*crystalline acid*)
Effective against a number of gram negative organisms and inhibits the growth of gram positive cocci.

Sobita (Howards)

Sodium bismuth tartrate

Yaws

Injection intramuscular 1-2 gm (15 4-30 8 gr) in 10% solution 2 c c (32 4 min)

Solganal B oleosum *Aurothioglucose*

Relapsing Fevers Lymphogranuloma inguinale clonorchiasis

Injection intravenous or intramuscular 0 1-0 4 gm (1 5-6 1 gr)

Soluseptasine B P C

Disodium p (γ phenylpropylamino) benzenesulphonamide-α-γ disulphonate

Filarial lymphangitis (*W bancrofti*)

Injection intravenous 1 gm (15 4 gr) in 10 or 20% solution.

Solustibosan *Sodium antimony gluconate Pentostam Sodium stibogluconas B P C*

A pentavalent antimony compound of hexonic acid

Kala azar Oriental Sore Espundia

Intravenous or intramuscular 6 c c contains 2% antimony (0 126 gm—1 8 gr) A course of 10 daily injections well tolerated

Solvochin

A 25% water soluble basic quinine preparation for intramuscular injection with pH adapted to reaction of tissues dissolved in phenazone

Malaria especially pernicious forms of subtertian

Intramuscular 2 2 c c (35 8 min) twice daily for 4 days maximum. Each ampoule contains 0 5 gm (7 7 gr) quinine Causes little local reaction

Sontochin *S N 6911, 3038 R P Sontoquine Santoquine*

(7 chloro 4 (4 diethylamino 1 methylbutylamino) 3 methylquinoline) disulphate and monohydrate salts

Malaria

Much used in Germany Dosage and action similar to that of chloroquine.

Stibamine

Sodium p aminophenylstibinate

Kala azar

Intravenous 0 1-0 2 gm (1 5-3 gr) total dosage 6-10 gm dissolved in 10 c c (2 7 3) distilled water on alternate days

Stibophenum B P

Fouadin Neoantimosan

Sodium antimony bispyrocatechol 3 5 sodium disulphonate

Contains 13 5% antimony in trivalent form

Schistosomiasis Lymphogranulome inguinale Leishmaniasis Filariasis

Intravenous and intramuscular 0 1-0 3 gm (1 5-4 6 gr) in 7% solution 1 5 c c 3 5 c c 5 c c (1 3 3) on consecutive days then 5 c c (1 3 3) on alternate days Total 40 c c (1 oz 2 3)

Stibosan Von Heyden 471

Sodium m-chlo-p-acetylaminophenylstibinate

Kala azar Rat bite Fever
Intravenous or intramuscular 0 2 gm (3 gr)
Total dosage 6–10 gm (92 5–154 gr) on alternate days

Stilbamidinæ Isethionas M & B 774 *Diamidino stilbene*

Used in form of B hydroxyethanesulphonate

Kala azar
Intravenous in *Indian* form—0 04 (0 6 gr) 0 075 (1 05 gr) 0 09 (1 35 gr) 0 12 (1 8 gr) 0 14 (2 1 gr) 0 15 gm (2 2 gr) in single course of 10–15 injections For children initial dose of 0 015 gm (0 22 gr)
Sudan form 1 3 5 mg per kg 15 daily injection separated by 7 day intervals Total dosage 3 4 8 gm (46 2 74 gr) Late neuropathies have frequently been reported after treatment

Stovarsol *Acetarsol B P Spirocid Acetarsone*

3-acetylamino 4 hydroxyphenylarsonic acid

Relapsing Fevers Rat bite Fever Trypanosomiasis Yaws Syphilis Tropical Eosinophilia Giardiasis Balantidiasis Trichomonas
Oral tab 0 06–0 25 gm (0 92 3 7 gr) two or three times daily for 10–12 days Prolonged treatment may give rise to arsenical poisoning

Streptomycini Sulphas B P Add

Antibiotic isolated from *Actinomyces griseus* employed as the sulphate
Meso 1 3-diguanidino 2 3 4 6 tetrahydroxy cyclo exane glucoside of a disaccharide

Active entirely against gram negative organisms
Tuberculosis Plague Tularæmia Ulcerating Granuloma of Pudenda Q Fever Bacillary Dysenteries *Bact coli* infections Meningitis Whooping Cough Actinomycosis and Gonorrhœa
Intramuscular in solution 0 5 gm of the base daily
Oral in cachets 250 mg (3 7 gr) four times daily for intestinal infections taken with a cup of milk or water
The following preparations are in use *Streptomycini et Calc chloridum Injectio Streptomycini et Calc chloridi Streptomycini Hydrochloridum Streptomycini sulphas* and *Injectio Streptomycini sulphatis*

Dihydro Streptomycinum (B P Add)

Consists of the hydrochloride or the sulphate

May be given to patients who have become sensitized to streptomycin
Causes more vestibular damage than parent substance Streptomycin is toxic to the vestibular branch of the 8th cranial nerve

Succinyl Sulphathiazolum B P *Sulphasuxidine Colistatin*

2(p succinyl amino benzenesulphonamido) thiazole

Bacillary Dysenteries Ulcerative Colitis
Oral tab or powder 10–14 gm (154–216 gr) Initial dose 4 gm followed by maintenance dose of 2 gm (30 8 gr) 4 times daily American workers advocate larger doses up to 0 25 gm (3 7 gr) per kg for pre and post operative treatment

Sulphadiazina B P

2 (p aminobenzenesulphonamido) pyrimidine

Pneumonia Plague Filariasis Bacillary Dysenteries Lymphogranuloma inguinale Melioidosis
Oral tab 1-4 gm (15 4-61 7 gr) Initial dose 4 gm (61 7 gr) followed by 1 gm every four hours Has low toxicity

Sulphadimidine B P *Sulphadimethylpyrimidine Sulphame athine*

2 (4 aminoben enesulphonyl amino 4 6 dimethylpyrimidine)

Pneumonia Bacillary Dysenteries Ulcerative Colitis
Oral tab 2 gm (30 8 gr) Initial dose = 1 gm (15 4 gr) Subsequently every 6 hours for 5-7 days

Sulphaguanidina B P *Sulphanylguanidine*

p aminoben enesulphonylguanidine monohydrate

Bacillary Dysenteries especially *S shigæ* infections
Oral tab 0 3 and 0 5 gm Individual dose -4 gm (30 8-61 7 gr)
Initial dose = 0 1 gm per kg Maintenance dose = 0 05 gm per kg
Total dosage in severe case = 130 gm (2006 gr)

Sulphamerazina B P C *Sulphamethydiazine*

Resembles sulphadia ine in general properties

Bact coli infections of the urinary tract for which its solubility mak specially suitable
Oral tab 0 5 gm (7 7 gr) For acute infections in adults 3-4 (46 2-61 7 gr) followed by 1 0 gm (15 4 gr) every 8 hours contir every 8 hours till clinical response is obtained
For children 3-10 years 1 5 gm (23 1 gr) followed by 1 gm (15 4 Under six months 0 5 gm (7 7 gr) followed by 0 25 gm (3 8 every 12 hours

Sulphapyridina B P C (*M & B* 693) *Sulphiadine*

2 (p aminoben enesulphamido) pyridine

Pneumonia Gonorrhœa Cerebrospinal meningitis Lymphogranulo inguinale Bubonic plague Streptococcal infections Dermatitis herp formis
Oral tab 0 5-2 gm (2 7-30 8 gr) followed by 1 gm (15 4 gr) 4 hou for 2 days then 1 gm (15 4 gr) 6 hourly for 2 days

Sulpharsphenamina B P *Myosalıarsan Sulpharsenol Sulphirsenoben* *Sulphostab*

Disodium 3 3 diamino 4 4 dihydroxyarsenobenzene N N dimethyls phate

Relapsing fever Yaws Syphilis Trypanosomiasis
Injection intramuscular or intravenous 0 1-0 6 gm (1 5-9 2 gr)

Sulphathiazolum B P *Thia amide Ciba ol*

- (p an inoben enesulphonamido) thiazole

Pneumonia Malaria Plague Filariasis Lymphogranuloma inguinale
Oral tab 2 gm (30 8 gr) initially 1 gm (15 4 gr) every 4 hours

Sulphatriad (*M & B*)

An association of sulphathiazole 0 37 gm (5 6 gr) sulphadiazine 0 37 gm (5 6 gr) and sulphamerazine 0 26 gm (3 9 gr) per gm for systemic sulphonamide therapy with reduced risk of crystalluria

Oral tab 2–4 gm (30 8–61 7 gr) Course as for other active sulphonamides

Sulphetrone *Solapsonum B P C*

Tetrasodium 4 4 di phenylpropyl amino diphenyl sulphone tetra sulphone

Leprosy Tuberculosis

Oral tab initial dose 1 5 gm (23 1 gr) gradually increasing to 6–9 gm (92 5–138 8 gr) daily

Toxic effects nausea vomiting depression drug rash and hypochromic anaemia frequently

Teropterin

Pteroyl γ glutamyl γ glutamyl glutamic acid

Sprue Pernicious Anæmia Carcinoma

Intramuscular injection 10–20 mg (0 15–0 3 gr) daily

Ampoules of 1 c c containing 10 mg (0 15 gr) injected daily for one week

Terramycinum *Oxytetracycline*

Antibiotic isolated from cultures of Streptomyces rimosus

Amœbiasis (chronic) Typhus Fevers Salmonella Infection *Bact coli* infections Oxyuriasis Balantidiasis Tropical Ulcer Yaws Anthrax Undulant Fevers

Oral capsules of 250 mg (3 7 gr) 2 gm daily (30 8 gr) in divided doses Treatment continued for 48 hours after temperature has become normal

Intravenous 0 5–1 gm daily in divided doses

Tetrachlorethylenum B P *Perchlorethylene Ethylene tetrachloride*

Ancylostomiasis Oxyuriasis *Hymenolepis nana*

Oral, capsules containing 1 c c (16 2 min)

Dose 1–3 capsules In liquid form 3 c c (48 6 min) prescribed with oil of chenopodium

Tetracycline *Achromycin Tetracyn Polycycline*

A broad spectrum antibiotic prepared by reduction from Aureomycin (*chlortetracycline*) (*q v*) Antibacterial activity similar to that of chlortetracycline and oxytetracycline but causes fewer side-effects and is more stable

Effective against numerous Gram positive and Gram negative organisms Undulant fevers Typhus Q fever Lymphogranuloma venereum Psittacosis Amœbiasis Yaws Coccidioidomycosis

Oral 250–500 mg 4 times daily

Injection intramuscular 200–300 mg daily in divided doses at 8–12 hour intervals intravenous 500 mg 12 hourly by drip as 0 1% solution

Tetraethyliurammonosulphide *Tetmosol*

Scabies

When combined with soap in 5–20% dilution it retains its sarcopticidal properties

Thiacetazonum *Thiosemicarbazone*

p acetylaminobenzaldehyde thiosemicarbazone

Tuberculosis Leprosy
Oral tab 0 1–0 2 gm (1 5–3 gr) daily
Injection dissolved in 1–2 c c (16 2–32 4 min) glycerin
Tolerated dose ≈ 2 mg per kg
Initial dose in leprosy sometimes as high as 50 mg (0 7 gr) increased over 4–8 weeks to 150 mg (2 2 gr)
Liable to produce toxic effects rashes and anæmia

Thio bismol *Bismuth Sodium Thio lycollate*

Benign Tertian Malaria
Injection intramuscular 0 2 gm (3 gr)

Thiomersal *Thiomersalate B P C Merthiolate Sodium ethylmercurithio salicylate*

Ringworm *Tinea circinata* etc
In form of ointment or in alcoholic solution 0 1 %

Thymol B P

3 methyl 6 isopropylphenol
Ancylostomiasis
Oral tab 3–4 gm (46 2–61 7 gr)

Totaquina B P

Mixture of cinchona alkaloids containing not less than 70% alkaloids of which not less than one fifth is quinine
Type I Quinine cinchonine cinchonidine
Type II Quinine quinidine cinchonine cinchonidine
Malaria
Oral tab 0 06–0 6 gm (0 9–9 2 gr) two to three times daily

Trichlorethylenum B P

Trilene
Ancylostomiasis Oxyuriasis
Oral liquid 2–3 c c (32 4–48 6 min) in capsules or mixture Contra indicated in heart or kidney disease

Triostam *Trivalent sodium antimonylgluconate*

Schistosomiasis *S hæmatobium S mansoni* and *S japonicum*
Intravenous 180 mg (2 7 gr) injected every day for 6 days 6% solution 15–20 mg (0 22–0 3 gr) per kg For man of 60 kg dosage 200 mg (3 gr) Oral can be given in 100 mg doses in enteric coated tablets
Solution must not be heated

Tryparsamidum B P *Tryparsone*

Sodium N phenylglycineamide-p arsonate
Trypanosomiasis *Trypanosoma gambiense T rhodesiense* Neurosyphilis
Intravenous or intramuscular injections
1–2 gm (15 4–30 8 gr) on alternate days or at definite intervals
Maximum 60 mg per kg
Total dosage 24 gm (369 8 gr)

Urea stibamine *Stiburea*

Combination of urea and p-aminophenylstibinic acid

Kala azar, other forms of Leishmaniasis, Filariasis, Schistosomiasis
Safer than tartar emetic
Intravenous or intramuscular ampoules of 50 (0.7 gr), 100 (1.5 gr) and 200 mg (3 gr). Dose 100–200 mg (1.5–3 gr) on alternate days

Vitamin B_{12} *Cyanocobalaminum B.P.C.* *Cytamen*

Pernicious Anæmia, Nutritional Macrocytic anæmia, Tropical Sprue, Macrocytic Anæmia of pregnancy
Intramuscular injection of 100 µmg

Win 5647 *Mantomide*

N-(2,4-Dichlorobenzyl)-N-(2-Hydroxyethyl) Dichloracetamide

Powerful amœbicide (*E. histolytica*)
Oral—under 5 years 250 mg (3.7 gr) t.d. for 8 days, 5–10 years 500 mg (7.7 gr) t.d. for 10 days, over 10 years 750 mg (11.5 gr) t.d. for 10 days

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